

**UNITED STATES PATENT AND TRADEMARK OFFICE**  
**CERTIFICATE OF CORRECTION**

**PATENT NO. :** 5,260,459

**DATED :** November 9, 1993

**INVENTOR(S) :** Ernst Joachim Brunke and Dietmar Schatkowski

It is certified that error appears in the above—identified patent and that said Letters Patent is hereby corrected as shown below:

In the cover sheet, after the Inventor block, insert block  
—[73] Assignee: Dragoco Gerberding & Co. GmbH  
Holzminden, Germany--

MAILING ADDRESS OF SENDER:

PATENT NO. 5,260,459

Certificate of Correction (PTO Form 1050)—Amended



This page Blank (uspbto)



US005260459A

**United States Patent** [19]**Brunke et al.**[11] **Patent Number:** **5,260,459**[45] **Date of Patent:** **Nov. 9, 1993**[54] **CYCLIC ISOLONGIFOLANONE-KETALS -  
THEIR MANUFACTURE AND THEIR  
APPLICATION**[76] **Inventors:** **Ernst-Joachim Brunke,**  
Pippingsbusch 3, Holzminden, 3450;  
**Dietmar Schatkowski,** Weststrasse 7,  
Stadtoldendorf 3457, both of Fed.  
Rep. of Germany[21] **Appl. No.:** **978,239**[22] **Filed:** **Nov. 18, 1992**[30] **Foreign Application Priority Data**

Nov. 19, 1991 [DE] Fed. Rep. of Germany ..... 413832

[51] **Int. Cl.:** ..... **C07D 317/92**[52] **U.S. Cl.:** ..... **549/336**[58] **Field of Search:** ..... **549/336**[56] **References Cited****U.S. PATENT DOCUMENTS**3,887,622 6/1975 Boelens et al. .  
4,331,569 5/1982 Inoue et al. .... 549/336  
4,774,225 7/1988 Giraudi ..... 549/336  
4,841,075 6/1989 Matsushita et al. .... 549/336**FOREIGN PATENT DOCUMENTS**2336798 1/1974 Fed. Rep. of Germany .  
1505821 3/1978 United Kingdom .**OTHER PUBLICATIONS**

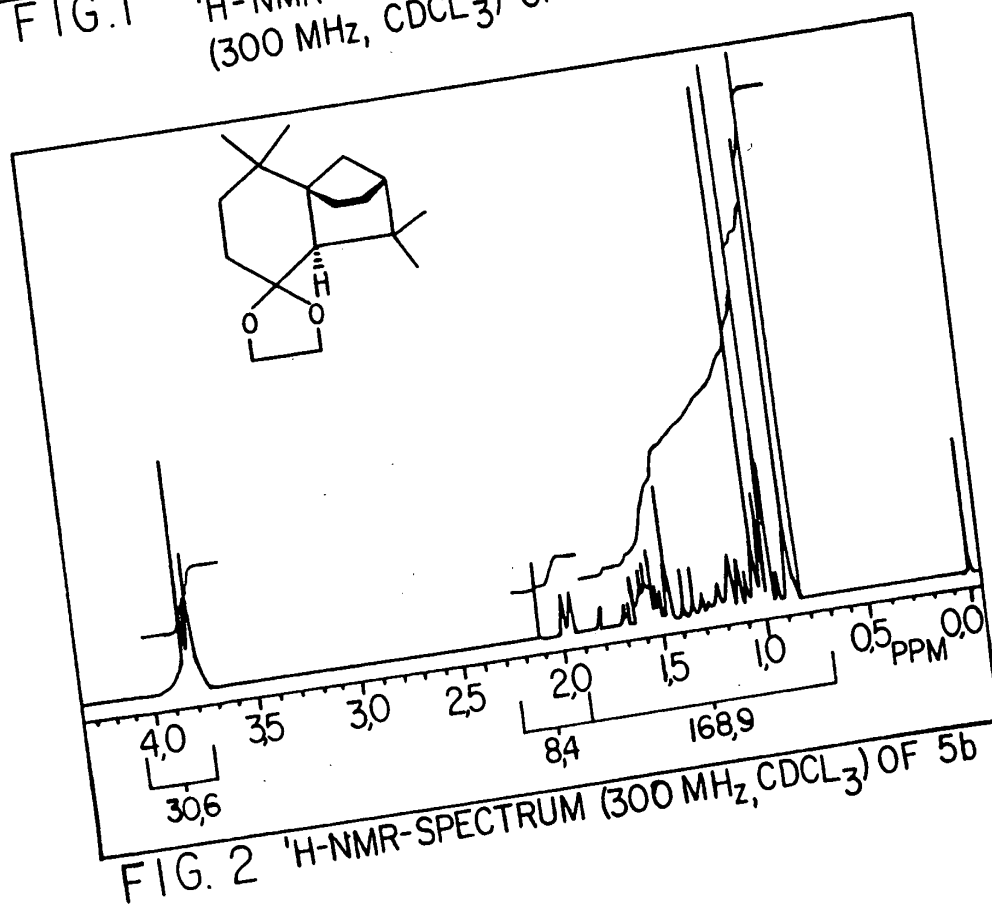
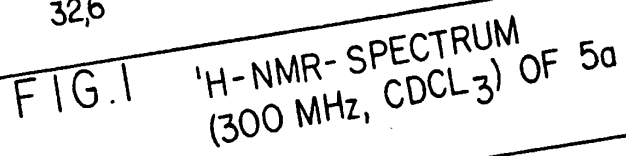
CA 81(5): 25442f (1974).

CA 89(7): 59977g (1978).

*Primary Examiner*—Marianne M. Cintins*Assistant Examiner*—John Peabody*Attorney, Agent, or Firm*—Dominik, Stein, Saccocio,  
Reese, Colitz & Van der Wall[57] **ABSTRACT**

The cyclic Isolongifolanone ketals of the general formula A wherein the wavy lines mean  $\alpha$  and  $\beta$ -configuration and R,R' mean radicals of hydrogen, methyl or ethyl, are new. With preference they are used either as odorants or as components of perfume compositions. They are manufactured from Isolongifolene which is itself produced from Longifolene as is well known. Isolongifolene is oxydized to Isolongifolene-3-on and this is reacted with aliphatic 1,2-diols in apolar solvents with the separation of water.

**6 Claims, 1 Drawing Sheet**



# CYCLIC ISOLONGIFOLANONE-KETALS - THEIR MANUFACTURE AND THEIR APPLICATION

Today, industrially manufactured perfume oils consist of synthetic odorants largely. The traditional application of essential oils or extracts of vegetable or animal origin is now mainly restricted to the area of alcoholic perfumery. Perfume for detergents, soaps, household cleaners and similar products requires the use of odorants which meet the technical demands of stability and substantivity. To comply with these demands, perfumes which are used in technical consumer products are essentially composed of synthetic odorants. Because these perfume oils are needed in large quantities as a result all major perfume companies and manufacturers of aroma chemicals have dedicated their research work over the last decades to produce new aroma chemicals.

It has become increasingly apparent during the last 10 years that synthetic odorants which were originally destined for the technical perfumery, and which due to their low prices and high stability were accordingly positioned in the market are now more and more used in the alcoholic perfumery. Perfumers have used their perfumistic know-how gained from the use of synthetic aroma chemicals in technical perfumes and applied it also to alcoholic perfumery as aesthetic chances may allow. Today, a successful new aroma chemical has to meet the following demands:

1. it has to present a high olfactory and aesthetic value and must be applicable in as wide a range of fragrance products as possible;
2. it has to be stable in most technical applications;
3. it has to show a good value-/for money-ratio;
4. it should be manufactured from generally available raw materials from renewable resources, whenever possible.

Such a raw material of natural origin available in large quantities is Longifolene (1) which is to be found as a main component in the Indian oil of turpentine and as a minor component in many other turpentine oils and other essential oils.

About 20 years ago, research laboratories of the aroma chemical industry produced a number of derivative products from Longifolene, which had odorant qualities. As reported in a summary by G. Ohloff in his book "Riechstoffe und Geruchssinn" (Springer-Verlag, Berlin, 1990, ISBN-Nr. 3-540-52560-2, pages 87-88) at least 4 commercial odorants are derived from the Longifolene (1). The Isolongifolene (2) which is obtained by the isomerization of Longifolene (1) can be proved to have fathered 13 commercial products. The chemistry and olfactory qualities of derivatives of the Isolongifolene (2) are summarized by G. Färber and H. Tan:

"Riechstoffe aus Isolongifolen", G. Färber, Parfümerie & Kosmetik, 68, 18 (1987)

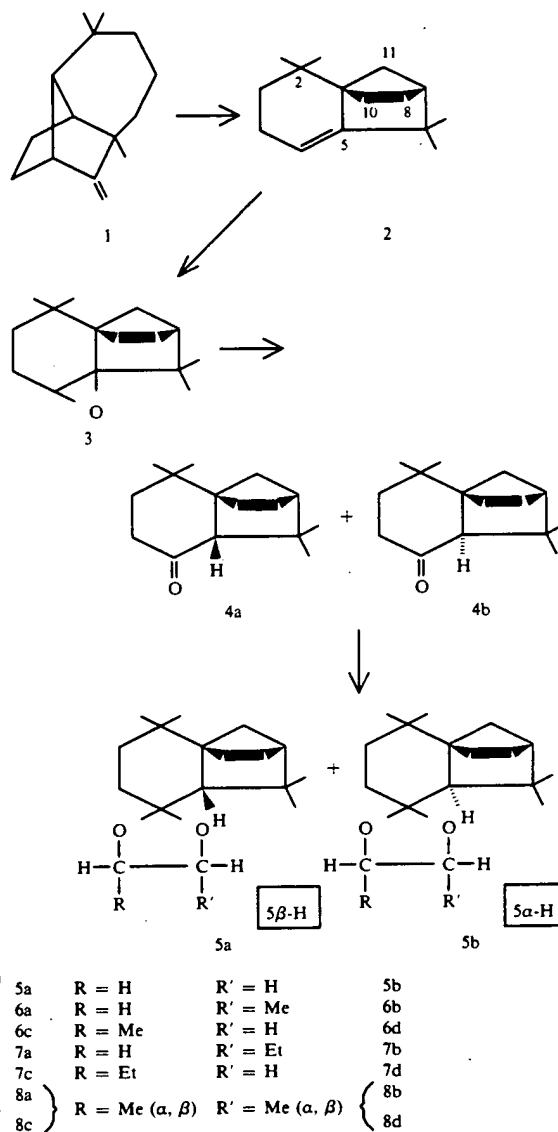
"Der Gebrauch von Riechstoffen aus Isolongifolenen in der Parfümerie", H. Tan, Parfümerie & Kosmetik, 67, 564 (1986)

The derivatives of Isolongifolene (2) obtained by epoxidation, Prins-reaction (reaction with formaldehyde) or allylic oxidation are considered olfactorily more valuable than the derivatives of Longifolene (1). They (2) are odorants of a warm-woody odor type, with some little amberlike aspects (Ohloff loc. cit.).

The epoxide (3) obtained by the reaction of Isolongifolene with peracids can be transferred as is known into mixtures of epimer ketones. The ketone mixtures

may contain different proportions of isomers with different odor effects. The ketone 4a is preferably manufactured in kinetic reaction while the ketone 4b is the thermodynamically more stable epimer.

According to the state of the art as described above, this area of the aroma chemical chemistry is considered to be especially well researched. Together with the derivatives of Longifolene and Isolongifolene which have useful odor qualities, a large number of other derivatives are known with little or no such value.



It is all the more surprising therefore, that new valuable odorants could be found in the area of the Longifolene derivatives such as the herewith claimed new cyclic acetals of the general formula A. The acetals of the general formula A present unique olfactory qualities clearly standing out from the known odorants derived from Isolongifolene (2) and superior to them. The new compounds of the general formula A present strongly woody olfactory qualities with flowery-fresh effects and with a velvety moss/ambra accent (see example 1); they are especially longlasting and act as fixatives.

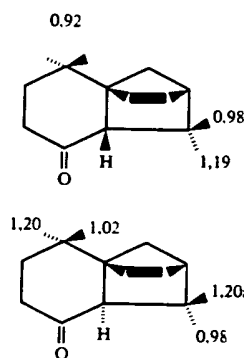
3

For the manufacture of compounds of the general formula A, Longifolene (1) has been treated as is well known with a mixture of acetic acid and sulphuric acid [U. R. Nayak, S. Dev, Tetrahedron 8, 42-48 (1960)] or with boron trifluoride-etherate [R. E. Beyler, G. Ourisson, J. Org. Chem. 30, 2838-2839 (1965)] to obtain Isolongifolene (2) by isomerization. The epoxide (3) [L. K. Lala, J. B. Hall, J. Org. Chem. 35, 1172, (1970); J. R. Prahlad, R. Ranganathan, W. Ramdas Nayak, T. S. Santhanakrishnan, S. Dev, Tetrahedron Lett. 8, 417 (1964)] obtained by epoxidation of Isolongifolene (2) has been transformed, as is well known, into the mixture of the epimer ketones 4a/4b [R. Ranganathan, U. R. Nayak, T. S. Santhanakrishnan, S. Dev, Tetrahedron 26, 621 (1970)]. In known conditions of the kinetic reaction the ring-opening of the epoxide produced a mixture of ketones 4a/4b concentrated in 4a (see example 2=96:4). It is known that 4a will be isomerized into the thermodynamically more stable ketone 4b under the influence of basic catalysts or by heating. Depending on the conditions of the reaction, mixtures of equilibrium of 4a/4b are obtained [L. K. Lala, J. Org. Chem. 36, 2560-2561 (1971)].

Our example 3 shows an isomerization not yet described to date leading from a mixture of ketones 4a/4b (96:4) to a specially highly concentrated mixture of equilibrium 4a/4b (9:91). The ketones 4a/4b have been isolated by distillation and chromatography and spectroscopically characterized. [C. W. Greengrass, R. Ramage, Tetrahedron 31, 689-694 (1975)].

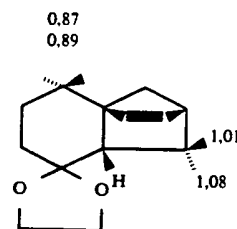
From ketones 4a, 4b which were present purely or in high concentration or in mixtures of equilibrium the new cyclic acetals of the formula A are produced as is known by the reaction with aliphatic 1,2-dioles in acidic catalysis with separation of water. The separation of water is preferably realized at boiling point with suitable inert solvents as carriers (examples 5-10).

If different solvents—toluene, cyclohexane, benzene fractions or n-pentane—are applied, the epimer ketals are produced in different proportions (example 5). So from 4a/4b (86:14) in example 2 under the effect of ethylene glycol in toluene the ketals 5a/5b have been obtained in the ratio of 3:2. When using n-pentane a ketal mixture 5a/5b was obtained after even a markedly prolonged reaction period. The ketals of formula A can be separated alternatively by distillation of the starting material 4a/4b if need be.

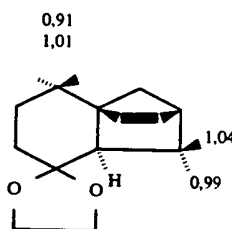


4

-continued



5a



5b

1H-NMR-Data,  $\delta$ [ppm]

The mixture equilibrated by basic catalysis of ketones 4a/4b (9:91, in example 3) had to undergo ketalisation reactions as well. Depending on the solvent used, different mixtures of 5a/5b were obtained, but which differed from the ketal mixtures 5a/5b obtained from the ketone mixtures 4a/4b (86:14, of example 2) so far as their relative concentrations were concerned. This varying reaction may be understood as kinetically controlled reaction during the ketalisation.

Analogues to the ketals 5a/5b the ketals 6a/6b/6c/6d were obtained by reaction of 4a/4b with 1,2-propandiol, the ketals 7a/7b/7c/7d with 1,2-butandiol, the ketals 8a/8b/8c/8d with 2,3-butandiol - each of them as a mixture. The methyl- or ethyl groups of the ketal radical may appear in an o- or B-configuration.

The compounds 5a, 6a, 6c, 7a, 7c, 8a, 8c are established as 5 $\beta$ -configured; the compounds 5b, 6b, 6d, 7b, 7d, 8b, 8d as 5 $\alpha$ -configured. Because starting from (+)-Longifolene the chiral ketals of the general formula A were obtained by means of the chiral ketones 4a/4b; 4a/4b exist as a mixture of epimers (5a/5b), respectively as diastereo isomers. 6a/6b and 7a/7b are constitutionally isomer to 6c/6d, respectively 7c/7d. Starting from (-)-Longifolene each of the enantiomer compounds 5a,b-8a-d are accessible.

Since both the composition of the ketal mixtures depends on the conditions of the reaction (example 5), and, the single diastereo isomers may be obtained in purity (examples 6, 7), the proportions within the mixtures may be adjusted to any level.

The attribution of the structure of the new compounds 5-8 has been based on the spectroscopical results (examples 5-10). The <sup>1</sup>H-NMR-spectra of the compounds 5a, 5b (designs 1, 2) have been interpreted in analogy to the attributions given by C. W. Green-grass and R. Ramage, Tetrahedron 31, 689 (1975) for the ketones 4a, 4b.

The new compounds of the formula A are well suited as odorants due to their olfactory qualities and their stability. They may be used successfully for perfume compositions of any fragrance type either as a main component or in traces to good avail. The examples quoted may not be understood as limitations.

## EXAMPLE 1

## Manufacture of Isolongifolene (2)

Over a period of 30 minutes 240 g (0.79 mol) of Longifolene (1) (80% ex Indian oil of turpentine [α]<sub>D</sub>+39.4°) were dropped into a heated solution (60° C.) of 90 g toluene and 10 g (0.07 mol) BF<sub>3</sub>-etherate. This was stirred at 100° C. for 3 hours, then cooled down to room temperature and neutralized. After drying above Na<sub>2</sub>SO<sub>4</sub> the solvent was distilled at reduced pressure. A raw product of 198 g (of 70.2% according to GLC) remained.

Gas chromatogram (HP 5890, DBWAX-30 N, 30 m, 150° C.—240° C., 8° C./min).

## EXAMPLE 2

## Manufacture of an Isolongifolanene mixture 4a/4b (86:14)

A threeneck-roundbottom-flask with jacketed coil condenser and dropping funnel was charged with 198 g (0.68 mol) Isolongifolene (2) (70.2% according to GLC) from example 1 plus 80 g toluene and 68 g (1.48 mol) formic acid and heated at 60°–70° C. Into this was dropped over a period of 1 hour 136 g (1.4 mol) H<sub>2</sub>O<sub>2</sub> at 35% concentration. After stirring for 3 hours at 80°–85° C. it was cooled to room temperature and worked up. The separated organic phase was neutralized with sodium carbonate solution and water, dried above Na<sub>2</sub>SO<sub>4</sub> and the solvent distilled at reduced pressure. 199 g raw product remained. GLC 4a (71%), 4b (2.5%) [96:4].

Distillation with a 15 cm Vigreux-column produced 165 g raw product of 4a/4b; b.p. 2 mm 120°–153° C. GLC: 4a (74%), 4b (3%).

A subsequent distillation with a column with metallic packing produced: 110 g 4a/4b (74.4% theoretical yield) b.p. 2 mm 137°–141° C.; GC 4a (77%), 4b (12.8%) [86:14].

D 20/4 = 1.0037

n 20/D = 1.5006

[α]<sub>D</sub>20/D = -8.5°

Gas Chromatogram: Conditions See Example 1

GLC/MS: HP 5970 DBWAX-60 N 60 m 60°–240° C. 4°/min 4a RT=40.47'

MS: m/e (%) = 220 (100, M<sup>+</sup>), 205 (41), 191 (82), 177 (41), 164 (62), 149 (50), 121 (56), 107 (40), 83 (27), 55 (21), 41 (17). 4b RT=41.41'

MS: m/e (%) = 220 (69, M<sup>+</sup>), 205 (23), 191 (55), 177 (44), 164 (100), 149 (55), 121 (53), 107 (37), 91 (21), 55 (21), 41 (19).

## EXAMPLE 3

## C-3-Epimerization of Isolongifolanone (4a/4b)

880 g (4 mol) raw (undistilled) ketone mixture 4a/4b from example 2 (purity according to GLC: 4a (63.3%), 4b (2.48%) [96:4]; 750 g methanol, 40 g (0.5 mol) NaOH 50% were charged into a three-neck-roundbottom-flask and stirred for 8 hours under reflux. After this period 30 g (0.5 mol) concentrated acetic acid were added to cool

down to room temperature. After the distillation of the solvent at reduced pressure the residual was mixed with water. The organic phase was then separated. The waterphase was extracted with 100 ml benzene. The mixed organic phases were washed first with sodium carbonate solution, then with water and dried above Na<sub>2</sub>SO<sub>4</sub>. The solvent was distilled at reduced pressure. 860 g dark brown oil remained.

GLC: 4a (6.3%), 4b (59.3%) [9:91]

## EXAMPLE 4

## C-3-Epimerization of pure Isolongifolanone (4a/4b)

440 g (2 mol) purely distilled ketone mixture 4a/4b from example 2 [purity according to GLC: 4a (77%), 4b (12.8%) [86:14]; 400 ml methanol, 20 g (0.25 mol) NaOH 50% were charged into a 2 l three-neck round-bottom-flask and stirred for 5 hours under reflux. After cooling to room temperature, 15.5 g (0.25 mol) concentrated acetic acid were added; the solvent was distilled at reduced pressure. The residual was then mixed with water. The organic phase was separated and the water phase was extracted with 100 ml benzene. The mixed organic phases were neutralized with sodium carbonate solution and water; after concentration 430 g brown oil remained.

GLC: 4a (9.2%), 4b (79.5%) [1:9]

Distillation in a 15 cm Vigreux-column produced 411 g 4a/4b (b.p. 2 mm 135°–157° C.). The subsequent distillation in a 40 cm column with metallic packing produced 399 g (90.7% theor. yield) 4a/4b b.p. 2 mm 139°–142° C.

GLC: 4a (13.4%), 4b (80.6%) [14:86]

D 20/4 = 1.0042

n 20/D = 1.5007

[α]<sub>D</sub> 20/D = -34.7°

## EXAMPLE 5

## Reaction of Isolongifolanone 4a/4b with ethylene glycol

220 g (0.6 mol) ketone mixture 4a/4b from example 2, 3 or 4, 186 g (3 mol) ethylene glycol, 1 g p-toluene sulfonic acid plus 300 ml solvent (toluene, cyclohexane, benzene (63°–80° C.), n-pentane) were charged in a 1 l three-neck-roundbottom-flask with water separator and heated at boiling point for 48–78 hours and stirred with water separation. During the reaction about 20 ml water each were separated at each stage. After cooling to room temperature, the mixture was neutralized with sodium carbonate solution and water, dried above Na<sub>2</sub>SO<sub>4</sub>, and the solvent distilled at reduced pressure 245–265 g raw product of either yellow or brown oil respectively were obtained.

Distillation with a 15 cm Vigreux-column produced 230 g raw 4a/4b (b.p. 2 mm 68°–170° C.). The subsequent distillation with a 40 cm column with metallic packing produced about 140 g (53% theor. yield) 5a/5b of light yellow oil.

Table 1 shows the results in a summary.

TABLE 1

Products of the reaction of 4a/4b with ethylenglycol/p-toluenesulfonic acid									
starting material (GLC-%)				Reaction		Composition of Product (GLC-%)			
a	+	4b	[4a/4b]	Solvents	Temp.	Time	4a	4b	[5a/5b]
a)	71%	2.5%	[96:4]	Benzene (63–80° C.)	70–72° C.	70 h	7.2	3.8	53.6 2.2 [96:4]
	71%	2.5%	[96:4]	Cyclohexane	90–92° C.	48 h	5.1	4.8	51.3 3.8 [93:7]
	71%	2.5%	[96:4]	Toluene	120° C.	24 h	1.2	10.4	37.8 19.6 [66:34]
(raw products from example 2)									
b)	77%	12.8%	[86:14]	n-Pentane	46–48° C.	84 h	17.1	11.1	60.1 0.8 [99:1]

TABLE 1-continued

Products of the reaction of 4a/4b with ethyleneglycol/p-toluenesulfonic acid									
starting material (GLC-%)				Reaction		Composition of Product (GLC-%)			
a	+	4b	[4a/4b] Solvents	Temp.	Time	4a	4b	5a	5b [5a/5b]
77%		12.8%	[86:14] Benzene (63-80° C.)	70-72° C.	72 h	1.8	14.6	57.9	14.3 [80:20]
77%		12.8%	[86:14] Cyclohexane	90-92° C.	25 h	2.4	10.0	65.5	11.3 [85:14]
77%		12.8%	[86:14] Toluene	120° C.	25 h	—	—	84.6	14.3 [86:14]
(Distillate from example 2)									
c)	6.3%	59.3%	[9:91] Benzene (63-80° C.)	70-72° C.	78 h	1.2	14.5	28.6	19.8 [59:41]
	6.3%	59.3%	[9:91] Cyclohexane	90-92° C.	78 h	2.1	11.5	36.9	13.6 [73:27]
	6.3%	59.3%	[9:91] Toluene	120° C.	78 h	2.9	8.4	37.7	13.3 [73:27]
(from example 3)									
d)	13.4%	80.6%	[14:86] Benzene (63-80° C.)	70-72° C.	72 h	—	22.9	35.6	35.1 [50:50]
	13.4%	80.6%	[14:86] Toluene	120° C.	48 h	1.5	3.3	67.9	19.8 [77:23]
(from example 4)									

## EXAMPLE 6

Manufacture of 5-ethylenedioxy-3 $\beta$ -H-isolongifolane (5a)

20 g purified ketal mixture from example 5b; (purity according to GLC: 5a (84.6%), 5b (14.3%) [86:14], were distilled once more for purification in a 1 m spinning band column. 2.8 g 5a as a light yellow oil were obtained, b.p. 2 mm 142°-143° C.

GLC: 5a (98%), 5b (0.8) [99:1]

D 20/4=1,0510

n 20/D=1,5051

GLC/MS: Conditions see example 2

5a RT 42.94'

MS: m/e (%) = 264 (23, M<sup>+</sup>), 249 (9), 235 (19), 195 (20), 165 (23), 127 (42), 99 (100), 55 (10).

<sup>1</sup>H-NMR: see design 1

<sup>13</sup>C-NMR (CDCl<sub>3</sub>), Varian VXR-300:  $\delta$  [ppm] = 21.86, 23.39, 26.79, 33.89 (CH<sub>3</sub>), 21.06, 25.75, 32.76, 35.89, 37.95, 61.84, 63.71 (CH<sub>2</sub>), 48.94, 52.48 (CH), 33.21, 37.67, 56.42, 112.23 (C).

## EXAMPLE 7

Isolation of 5-ethylenedioxy-3 $\alpha$ -H-isolongifolane (5b)

1 g of raw ketal mixture from example 5d (purity according to GLC: 5a (35.6%), 5b (35.1%) [1:1]) was purified by repeated (3 $\times$ ) flash-chromatography.

## Conditions of Chromatography

150 g silica gel 60, Grain size 0.04-0.063 mm., (Merck, Art.-No. 9385).

Solvent Benzene/Ethyl acetate = 95/5

Weight: 1 g

Yield: 78 mg; GLC: 5a (3%), 5b (90%) [3:97]

GLC/MS: Conditions See Example 2

5b RT 44.67'

MS: m/e (%) = 264 (9, M<sup>+</sup>), 249 (1), 235 (1), 221 (2), 191 (1), 149 (2), 127 (9), 99 (100), 55 (6), 41 (3).

<sup>1</sup>H-NMR: see design 2

<sup>13</sup>C-NMR (CDCl<sub>3</sub>), Varian VXR-300:  $\delta$  [ppm] = 25.51, 26.72, 26.93, 31.09 (CH<sub>3</sub>), 26.01, 30.41, 31.65, 36.90, 37.56, 61.38, 63.05 (CH<sub>2</sub>), 49.53, 56.89 (CH), 32.46, 40.99, 56.63, 111.78 (C).

## EXAMPLE 8

## Manufacture of

5-(1'-Methylethylenedioxy)-isolongifolane 6a/6b/6c/6d 65  
440 g (2 mol) of purified ketone mixture 4a/4b from example 2; (purity according to GLC: 4a (77%), 4b (12.8%) [86:14], 760 g (10 mol) propylene glycol-1,2,

600 ml toluene, 2 g p-toluene sulfonic acid were charged into a 4 l three-neck-roundbottom-flask with water separator. The mixture was stirred for 30 hours under reflux. After cooling to room temperature it was neutralized with sodium carbonate solution and water, dried above Na<sub>2</sub>SO<sub>4</sub> and the solvent was distilled at reduced pressure. 540 g of light brown raw product remained.

Distillation with a 15 cm Vigreux-column produced 298 g (53.6% theor. yield) 6a/6b/6c/6d; b.p. 2 mm 158°-162° C.).

GLC/MS: Conditions See Example 2

RT 41.11'

MS: m/e (%) = 278 (21, M<sup>+</sup>), 263 (19), 249 (40), 179 (41), 141 (39), 113 (100), 83 (20), 55 (31).

RT 42.03'

MS: m/e (%) = 278 (29, M<sup>+</sup>), 263 (22), 249 (55), 209 (40), 179 (49), 141 (42), 113 (100), 83 (21), 55 (31).

RT 42.11'

MS: m/e (%) = 278 (23, M<sup>+</sup>), 263 (21), 249 (44), 209 (35), 179 (47), 141 (39), 113 (100), 83 (21), 55 (34).

RT 42.47'

MS: m/e (%) = 278 (29, M<sup>+</sup>), 263 (21), 249 (51), 209 (37), 179 (47), 141 (44), 113 (100), 83 (21), 55 (26).

## EXAMPLE 9

## Manufacture of

5-(1'-Ethyl-ethylenedioxy)-isolongifolane 7a/7b/7c/7d

220 g (1 mol) purified ketone mixture 4a/4b from example 2 (purity according to GLC: 4a (77%), 4b (12.8%) [86:15], 270 g (3 mol) 1,2-butandiol, 300 ml cyclohexane, and 1 g p-toluene sulfonic acid were charged into a 1 l three-neck-roundbottom-flask with water separator. The mixture was stirred for 50 hours. After cooling to room temperature it was then neutralized with sodium carbonate solution and water and dried above Na<sub>2</sub>SO<sub>4</sub>. After distillation of the solvent at reduced pressure 328 g of light brown oil remained.

A subsequent distillation with a 15 cm Vigreux-column produced 195 g (66.8% theor. yield) 7a/7b/7c/7d; b.p. 2 mm 152°-157° C. as light yellow oil.

GLC/MS: Conditions See Example 2

Rt 42.55'

MS: m/e (%) = 292 (16, M<sup>+</sup>), 277 (15), 263 (37), 223 (27), 193 (28), 155 (26), 127 (100), 83 (13), 55 (43).

Rt 43.37'

MS: m/e (%) = 292 (32, M<sup>+</sup>), 277 (25), 263 (56), 223 (48), 193 (41), 155 (37), 127 (100), 83 (17), 55 (49).

Rt 43.66'

MS: m/e (%) = 292 (19, M<sup>+</sup>), 277 (19), 263 (42), 223 (45), 193 (34), 155 (28), 127 (100), 83 (13), 55 (50).

Rt 44.29'

MS: m/e (%) = 292 (32, M<sup>+</sup>), 277 (24), 263 (57), 223 (43), 193 (41), 155 (43), 127 (100), 83 (17), 55 (50).

#### EXAMPLE 10

Manufacture of 5-(1',2'-dimethyl-ethylene dioxy)-isolongifolane 8a/8b/8c/8d

220 g (1 mol) of purified ketone mixture 4a/4b from example 2 (purity according to GLC: 4a (77%), 4b (12.8%) [86:14]; 270 g (3 mol) 2,3-butandiol, 300 ml cyclohexane, and 1 g p-toluene sulfonic acid were charged into a 1 l three-neck-roundbottom-flask and stirred for 50 hours under reflux. After cooling to room temperature it has been neutralized with sodium carbonate solution and water and dried above Na<sub>2</sub>SO<sub>4</sub>. The solvent was distilled at reduced pressure. 275 g 20 light brown raw product remained.

Distillation with a 15 cm Vigreux-column produced 211 g (72.2% theor. yield) 8a/8b/8c/8d; b.p. 2.5 mm 158°-162° C. as a light yellow oil.

D 20/4 = 1.0115

n 20/D = 1.4975

GLC/MS: Conditions see example 2

Rt 39.69'

MS: m/e (%) = 292 (41, M<sup>+</sup>), 277 (25), 263 (57), 223 (50), 193 (49), 155 (50), 127 (100), 83 (20), 55 (29).

Rt 40.14'

MS: m/e (%) = 292 (47, M<sup>+</sup>), 277 (30), 263 (63), 223 (59), 193 (53), 155 (51), 127 (100), 83 (20), 55 (35).

Rt 42.76'

MS: m/e (%) = 292 (16, M<sup>+</sup>), 277 (14), 263 (28), 223 (28), 193 (26), 155 (25), 127 (100), 83 (15), 55 (28).

Rt 43.36'

MS: m/e (%) = 292 (56, M<sup>+</sup>), 277 (40), 263 (91), 223 (78), 193 (66), 155 (64), 127 (100), 83 (38), 55 (41).

#### EXAMPLE 11

Description of Odours of Ketals 5 to 8

The olfactory qualities of the materials at 10% in 45 Ethanol have been evaluated by a group of experts using smelling strips. Their findings were as follows:

5a/5b [86:14] from example 5b:

strong, sweet-woody, with a velvety-ambra accent and flowery aspects.

5a from example 6:

strongly woody with a mossy ambra-accent and a fresh effect.

5b from example 7:

woody, light flowery, with a softly earthy ambra note, a bit weaker than compound 5a.

6a/6b/6c/6d (from example 8):

strongly woody, powdery, with a fresh ambra accent.

7a/7b/7c/7d (from example 9):

dry, woody

8a/8b/8c/8d (from example 10):

strongly woody, with aspects of mossy, earthy and sweet-animal notes.

The odors of all compounds were found to be extremely longlasting and could be smelled after several weeks.

#### EXAMPLE 12

Perfume Base of a Flowery-woody Type

Oil of bergamot	7.5
Linalool	4.0
Phenyl ethyl alcohol	5.0
Benzyl acetate	2.0
Citronellol	2.0
Hedione ® (a)	10.0
Lyrall ® (b)	4.0
Hydroxycitronellal	2.5
Roseoxide 1 (c) 10% in DPG	2.5
Hexyl cinnamic aldehyde, alpha	7.5
Patchouly Oil Indonesian	4.0
Iso-E-Super ® (b)	2.0
Vetiveryl acetate	2.0
Brahmanol ® F (c)	2.0
Benzylsalicylat	2.0
cis-3-Hexenylsalicylat	1.0
Cedramber ® (b)	1.0
Musk Xylene	1.0
Indole 10% in DPG	0.5
Extract of Opoponax	0.5
Extract of Oakmoss 50% in DPG	5.0
	68.0

(a) Firmenich

(b) IFF

(c) DRAGOCO

The perfume base of the indicated formula presents a well balanced flowery-woody character which may be markedly amplified and harmonized by addition of 32 parts of 5a/5b (80:20).

#### EXAMPLE 13

Perfume Base of the Fougère Type

Oil of bergamot	18.0
Oil of Lavandin Super	15.0
Lilial ®	10.0
p-anisaldehyde	3.0
Coumarin	5.0
Hexyl cinnamic aldehyde, alpha	20.0
Ambrinol epoxide 10% in DPG	0.5
Ambroxan ® (d) 10% in DPG	1.0
Romaryl ® (c)	10.0
Peppermint oil	1.0
	82.5

(c) DRAGOCO

(d) Henkel

The perfume base of the indicated formula shows a fresh herbal fougère odor. An addition of 7.5 parts 6a/6b/6c/6d smoothes the composition and puts an accent on the ambra-woody note. Alternatively, an addition of 7.5 parts 8a/8b/8c/8d also smoothes the composition but puts the accent on an animal woody aspect.

#### EXAMPLE 14

Oil of Galbanum ED	0.5
Eugenol	1.0
Methylnone-gamma	5.0
cis-3-Hexenylsalicylat	6.0
Benzyl acetate	8.0
Lignofix ® (c)	5.0
Hedione ® (a)	10.0
Benzylsalicylat	10.0

-continued

Hexyl cinnamic aldehyde, alpha	12.0	5
Phenyl ethyl alcohol	15.0	
	72.5	

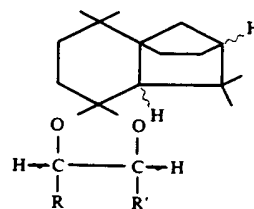
(a) Firmenich

(c) DRAGOCO

The perfume oil of the indicated formula shows a harmonic flowery green character. Alternative addition of either 7.5 parts 5a/5b or 7a/7b/7c/7d produces a very desirable balancing in a very natural effect.

We claim:

1. Cyclic isolongifolanone ketals of the general formula (A) wherein the wavy lines mean  $\alpha$ - and  $\beta$ -configuration and R and R' independently mean radicals selected from the group consisting of hydrogen, methyl or ethyl



2. Cyclic isolongifolanone ketals as in claim 1, wherein R and R' represent hydrogen.

3. Cyclic isolongifolanone ketals as in claim 1, wherein R represents hydrogen and R' represents methyl, or R represents methyl and R' represents hydrogen.

4. Cyclic isolongifolanone ketals as in claim 1, wherein R represents hydrogen and R' represents ethyl, or R represents ethyl and R' represents hydrogen.

5. Cyclic isolongifolanone ketals as in claim 1, wherein R and R' represent methyl ( $\alpha, \beta$ ).

6. Cyclic isolongifolanone ketals as in claim 1, wherein said ketals are produced by the process comprising obtaining isolongifolene from longifolene, oxidizing isolongifolene to isolongifolene-3-one and reacting with aliphatic 1,2-dioles in an apolar solvent accompanied by separation of water.

\* \* \* \* \*

## United States Patent [19]

Inoue et al.

[11]

4,331,569

[45]

May 25, 1982

[54] **SUBSTITUTED NORBORNANONE  
ACETALS, PROCESS FOR PREPARING THE  
SAME, AND PERFUME COMPOSITIONS  
CONTAINING THE SAME**

[75] Inventors: Yoshiharu Inoue, Ohsaka; Fumio  
Tanimoto, Kyoto; Hisao Kitano,  
Ohsaka, all of Japan

[73] Assignee: Nippon Petrochemicals Co., Ltd.,  
Japan

[21] Appl. No.: 220,528

[22] Filed: Dec. 29, 1980

[30] Foreign Application Priority Data

Dec. 29, 1979 [JP]	Japan	54-172063
Feb. 21, 1980 [JP]	Japan	55-6060
May 13, 1980 [JP]	Japan	55-63116
May 14, 1980 [JP]	Japan	55-63677

[51] Int. Cl.<sup>3</sup> ..... A61K 7/46; C07D 319/04;  
C07D 317/10

[52] U.S. Cl. .... 252/522 R; 549/336

[58] Field of Search ..... 260/340.9 R, 340.7,  
260/338; 252/522 R

[56] References Cited

## U.S. PATENT DOCUMENTS

3,634,499	1/1972	Loeffler	260/340.9 R
3,679,756	7/1972	Kretschmar et al.	260/340.9 R

3,748,344	7/1973	McCloud et al.	260/340.9 R
3,860,635	1/1975	Kitchens	252/522 R

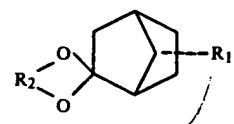
Primary Examiner—Ethel G. Love

Attorney, Agent, or Firm—Ostrolenk, Faber, Gerb &  
Soffen

[57]

## ABSTRACT

The substituted norbornanones represented by general  
formula (I):



(I)

(wherein R<sub>1</sub> is an alkenyl group having 2 or 3 carbon atoms or an alkylidene group having 1 to 3 carbon atoms and R<sub>2</sub> is a saturated hydrocarbon group having 2 to 7 carbon atoms with the dotted line between the two carbon atoms indicating a single bond when R<sub>1</sub> is an alkenyl group and a double bond when R<sub>1</sub> is an alkylidene group) are useful for perfume compositions. The substituted norbornanones represented by the general formula (I) may be prepared from the corresponding alkenyl or alkylidene norbornanones with diols in the presence of an acid catalyst.

18 Claims, No Drawings

This Page Blank (uspto)

# SUBSTITUTED NORBORNANONE ACETALS, PROCESS FOR PREPARING THE SAME, AND PERFUME COMPOSITIONS CONTAINING THE SAME

## BACKGROUND OF THE INVENTION

### 1. Field of the Invention

The present invention relates to novel derivatives of substituted norbornanones, specifically, alkenyl norbornanones or alkylidene norbornanones, a process for preparing the same, and a perfume composition containing the same.

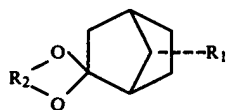
### 2. Description of the Prior Art

A variety of compounds having the norbornane ring have been heretofore prepared. For example, U.S. Pat. No. 3,860,635 discloses a process for preparing vinyl norbornanones. Similarly, U.S. Pat. No. 3,748,344 discloses a process for preparing cyclic acetals of norbornane carboxyaldehydes.

## SUMMARY OF THE INVENTION

It has been found that alkenyl or alkylidene norbornanones can be reacted with diols to give novel acetal compounds which have pleasant fragrances and are useful as components for providing the fragrance of a perfume, and that their acetal compounds can be employed effectively as intermediate compounds for organic synthesis and as raw materials for synthetic resins by utilizing an unsaturated group such as the ethylidene group or the vinyl group. The present invention was completed on the basis of this finding.

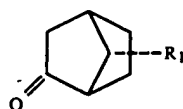
Thus, the present invention includes compounds represented by the following general formula:



(wherein R<sub>1</sub> is an alkenyl group having 2 or 3 carbon atoms or an alkylidene group having 1 to 3 carbon atoms, and R<sub>2</sub> is a saturated hydrocarbon group having 2 to 7 carbon atoms, with the dotted line between the two carbon atoms indicating a single bond when R<sub>1</sub> is an alkenyl group and a double bond when R<sub>1</sub> is an alkylidene group); a process for preparing the compounds represented by the above general formula (I) characterized by reacting an alkenyl or alkylidene norbornanone with a diol in the presence of an acid catalyst at a temperature of 10° C. to 150° C.; and a perfume composition containing the compounds represented by the general formula (I).

## DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

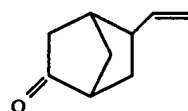
The alkenyl or alkylidene norbornanones to be used for the process in accordance with the present invention may be represented by general formula (VI):



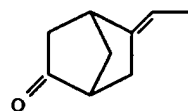
(wherein R<sub>1</sub> is an alkenyl group having 2 or 3 carbon atoms or an alkylidene group having 1 to 3 carbon atoms, with the dotted line between the carbon atoms indicating a single bond when R<sub>1</sub> is an alkenyl group and a double bond when R<sub>1</sub> is an alkylidene group).

The alkenyl group may include vinyl, propenyl, isopropenyl and allyl groups or the like. The alkylidene group may include methylene, ethylidene, propylidene and isopropylidene groups or the like.

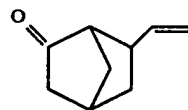
For example, when R<sub>1</sub> is a vinyl group or an ethylidene group, the compounds of formula (VI) may be represented by the following formulae (IV)-1, (IV)-2, (V)-1 and (V)-2:



(IV)-1

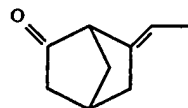


(IV)-2



(V)-1

and



(V)-2

In accordance with the present invention, the alkenyl or alkylidene norbornanones represented hereinabove may be used singly or in a mixture of two or more.

The alkenyl norbornanones represented hereinabove may be prepared readily by adding an acid such as sulfuric acid, formic acid, acetic acid or the like to the alkenyl norbornenes such as vinyl norbornene; hydrolyzing the resulting products to give the alkenyl norbornanols; and then oxidizing them to the alkenyl norbornanones. The alkenyl norbornene such as vinyl norbornene (5-vinyl-bicyclo [2.2.1] hept-2-ene) may be readily prepared on an industrial scale and at a low cost by means of the Diels-Alder reaction between cyclopentadiene and butadiene.

The alkylidene norbornanones represented hereinabove may be likewise prepared readily by adding an acid such as sulfuric acid, formic acid, acetic acid or the like to the alkylidene norbornenes such as ethylidene norbornene and hydrolyzing the resulting compounds; or by subjecting the alkylidene norbornenes to hydroboration-hydrogen peroxide oxidation to produce the corresponding ethylidene norbornanols; and then oxidizing the alcohols. It is to be noted, however, that the process including the step of adding the organic acid as mentioned hereinabove provides a large amount of tricyclene-type by-products which are less useful in perfumes, in addition to ethylidene norbornanol. These by-products are not readily separated by a usual distillation operation, so that it is preferable to produce ethylidene norbornanol by utilizing the hydroboration method.

This Page Blank (uspto)

The ethylidene norbornene (5-ethylidenebicyclo[2,2,1]hept-2-ene) can be readily prepared on an industrial scale and at a low cost as a third copolymeric component for EP rubber by isomerization of the vinyl norbornene represented hereinabove.

The diols to be used for the process in accordance with the present invention to convert the alkenyl or alkylidene norbornanones to the corresponding acetals may be a 1,2-diol or a 1,3-diol.

The term "1,2-diol" referred to herein means a compound in which two hydroxyl groups are attached respectively to two adjacent carbon atoms of a saturated hydrocarbon. The term "1,3-diol" referred to herein means a compound in which two hydroxyl groups are attached respectively to two carbon atoms of a saturated hydrocarbon, with another carbon atom interposed between the said carbon atoms.

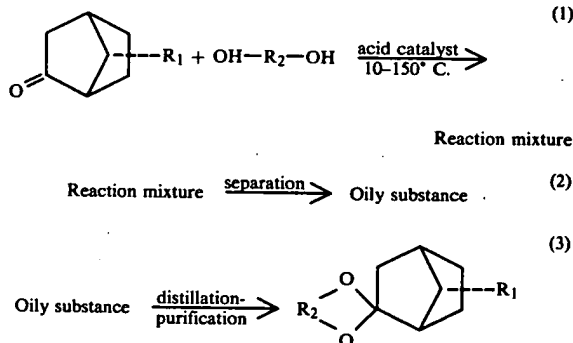
Representatives of the 1,2-diols stated hereinabove may be ethylene glycol, 1,2-propanediol, 1,2-butanediol, 1,2-, 2,3- or 3,4-hexanediol, 1,2- or 2,3-pentanediol, 1,2-cyclohexanediol, 1,2-methylcyclohexanediol and the like.

Illustrative of the 1,3-diols may be 1,3-propanediol, 1,3-butanediol, 2,2-dimethyl-1,3-propanediol, 2,2-diethyl-1,3-propanediol, 2-methyl-1,3-propanediol, 2-ethyl-1,3-propanediol, 1,3-cyclohexanediol, 1,3-methylcyclohexanediol and the like.

In the reaction in which the corresponding acetals are formed, the diols represented hereinabove may be used singly or in a mixture.

When the diols are represented by the formula:

HO—R<sub>2</sub>—OH, the process in accordance with the present invention may be represented by the following steps:



The reaction in the step (1) to be carried out in the presence of an acid catalyst involves a risk when carrying out the reaction at high temperatures using a large amount of a strong acid catalyst, because the unsaturated hydrocarbon group R<sub>1</sub> should not undergo any transformation. Thus, it is necessary to choose a reaction condition which does not cause polymerization.

The acid catalysts may include, for example, sulfuric acid, hydrochloric acid, hydrobromic acid, hydrofluoric acid, fluorosulfonic acid, chlorosulfonic acid, methanesulfonic acid, toluenesulfonic acid, boron fluoride hydrate, phosphoric acid, polyphosphoric acid, trichloroacetic acid, trifluoroacetic acid, perfluoroaliphatic acid, a strong-acid ion exchange resin, anhydrous phosphoric acid, anhydrous boric acid, acid clay and the like. Furthermore, the acid catalyst may be employed singly or in a mixture of two or more. However, care should be taken to avoid the use of a compound, such as boron fluoride, aluminum chloride, iron chlo-

ride, anhydrous sulfuric acid, very strong acids and so on in an anhydrous reaction system, which may cause a side-reaction. In order to carry out the reaction in the step (1) above, the reaction temperature is in the range of 10° C. to 150° C., preferably 30° C. to 100° C., and more preferably, 60° C. to 90° C. When the reaction temperature is below 10° C., the reaction requires a large amount of the acid catalyst and a long period of reaction time, thereby causing side-reactions other than the acetal formation and producing a large amount of, for example, polymerized products, and consequently decreasing the yield of the desired product. When the reaction is carried out at a temperature of higher than 150° C., the addition of the acid catalyst to the unsaturated hydrocarbon group R<sub>1</sub> takes place, thereby reducing the yield of the desired product.

The reaction of step (1), acetalization, requires removing the by-produced water to accelerate the acetal reaction.

Accordingly, it is preferred to carry out the acetal reaction under reflux with a solvent which can form a minimum boiling azeotrope with water and is inert in the acetal reaction. Such solvents may include, for example, benzene or toluene. It is also preferred to employ a solvent in order not to cause any conversion of the unsaturated bond during the acetal reaction.

In the process for preparing the norbornanone acetals in accordance with the present invention, the molar ratio of the alkenyl or alkylidene norbornanone to the diol to be used for the acetal formation is in the range of 1:0.5 to 1:3, and preferably, 1:1 to 1:2.

The amount of the acid catalyst represented hereinabove to be used in the acetal formation is in the range of 0.01 to 10% by weight, and preferably, 0.5 to 5% by weight with respect to the raw materials in the reaction system.

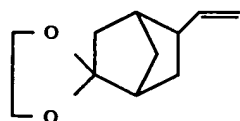
The reaction in the step (1) permits easy separation of the acetal from the reaction mixture when a usual alcohol (monoalcohol) is employed. However, the use of the diols as mentioned in the present invention requires some improvement or modification to isolate the desired product. The steps of acquiring the desired compound are represented by the steps (2) and (3) above. The oily substance of the step (2), which is a crude product, is first separated from the reaction mixture obtained in the step (1) under as moderate reaction conditions as possible. For this purpose, the separation may be carried out by extraction with an organic solvent from a mixture of the reaction mixture in water, by salting out, or by decantation, solution separation or centrifugation of a mixture of the reaction mixture in a solvent (such as water, ethylene glycol, Freon or the like) which does not completely dissolve the reaction mixture. When non-oily materials such as crystalline substances, rubbery substances or resinous substances are mixed in the reaction product during the course of separation, they must be removed as much as possible. It is appropriate that other non-oily materials such as water, organic solvents soluble in water, and so on may be removed by drying, evaporation, concentration of adsorption procedures. The oily substance thus obtained is then purified by distillation purification as represented in the step (3). Purification procedures other than distillation procedures cannot improve the quality of the desired product and decrease its yield. Accordingly, in order to facilitate purification by atmospheric-pressure distillation, reduced-pressure distil-

*This Page Blank (uspto)*

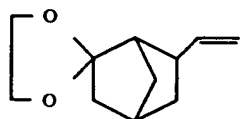
lation, molecular distillation or the like, it is necessary to choose an appropriate raw material diol. Where purification by distillation cannot be effected because the desired product solidifies or is rendered waxy due to the use of a large molecular-weight diol, the separation of impurities cannot be accomplished. Thus, due attention should be paid to the choice of the raw material. In many cases, the method for purification by distillation is reduced-pressure fractional distillation (reduced pressure rectification). When the distillation results in complete purification, the alkenyl norbornanone acetals in accordance with the present invention may be obtained as colorless, transparent liquids.

The alkenyl or alkylidene norbornanone acetals in accordance with the present invention prepared as described hereinabove may be represented by the general formula (I) above. The acetal formation using the 1,2-diol results in the formation of the 1,3-dioxolane ring; that using the 1,3-diol results in the formation of the 1,3-dioxane ring.

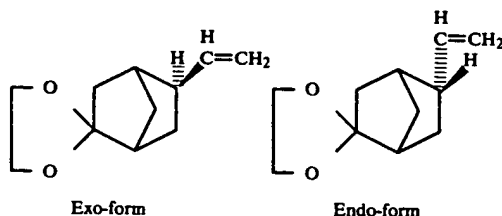
Thus, the acetal formation from 5-vinyl-2 or 3-norbornanone and ethylene glycol results in the formation of vinylnorbornanone ethyleneacetal {2-(5-vinyl-norborn-2' or 3'-yl)-1,3-dioxolane} represented by the following formula:



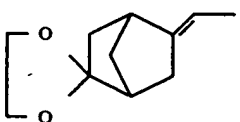
or



Since the carbon atom to which the alkenyl group such as the vinyl group or the like is attached has a hydrogen atom, there are two kinds of stereoisomers, the exo and endo-forms. They may be represented for the above 5-vinyl-2-norbornanone ethyleneacetal as follows:

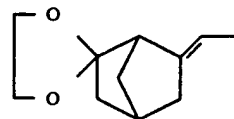


The acetal formation from 5-ethylidene-2 or 3-norbornanone and ethylene glycol results in the formation of ethylidene norbornanone ethyleneacetal or spiro[1,3-dioxolane-2,2' or 2,3'-(5'-ethylidenenorbornane)] represented by the following formula:



-continued

or



The alkenyl or alkylidene norbornanone acetals in accordance with the present invention are useful as perfume compositions because they have a desirable fragrance. Since the unsaturated groups such as the vinyl group or the ethylidene group can be utilized for further synthetic reactions, they can be used as useful intermediate products or raw materials for synthetic resins in the synthetic chemical industry.

Since the ethylidene norbornene is obtainable in a large amount and at a low cost as a third copolymeric monomer of EP rubber as stated hereinabove, it is economically advantageous to use as a starting material ethylidene norbornanone resulting from the oxidation of this ethylidene norbornene with the aid of the hydroboration method. This starting material does not contain any tricyclic-type compounds therein so that its usefulness in a perfume can be further enhanced.

Since vinyl norbornene is readily and cheaply available as an intermediate product for the manufacture of ethylidene norbornene for use in EPDM, it is economically advantageous to employ it as a starting material for the alkenyl norbornanone obtainable by acid addition, hydrolysis and oxidation.

Although the norbornene-type compounds in accordance with the present invention have a woody fragrance as a keynote, they may be favorably formulated with floral notes, fougere notes, mossy notes, chypre notes, leather notes, tobacco notes, animal notes, citrus notes, resinous notes, green notes, fruity notes, aldehydic notes, ester notes or the like to thereby provide various favorable perfume compositions. The perfume compositions may be employed as agents for providing fragrance in various perfumes, cosmetics, soaps, household products or the like. They may also be used extensively as flavor components, artificial essential oil components, deodorant components, perfume extender or the like.

The following examples illustrate the present invention in more detail.

#### Preparation Example 1

##### Synthesis of 5-vinyl-2 or 3-norbornanone

One mole of 5-vinyl-2-norbornene (5-vinyl-bicyclo[2.2.1]hept-2-ene) was mixed with 4 moles of 98% formic acid and the mixture was stirred at 50°-70° C. for 4 hours. The unreacted formic acid was first recovered by reduced pressure distillation and then an ester having a boiling point of 104°-105° C./22 mmHg,  $n_D^{14} = 1.4821$  (2- or 3-formoxy-5-vinylnorbornene) was obtained in a yield of about 62%.

One mole of the resulting ester and 1.2 moles of sodium hydroxide (used as a 10% aqueous solution) were mixed with methanol and the mixture was boiled for 2 hours to yield a reaction mixture which in turn was saturated with salt and then extracted with an etherbenzene mixture. The extract was dried over anhydrous magnesium sulfate and subjected to precision distillation to give an alcohol (5-vinyl-2 or 3-norbornanol)

*This Page Blank (uspto)*

having a boiling point of 85° C./4 mmHg,  $n_D^{14} = 1.5020$  in a yield of over 90%.

A sulfuric acid solution of chromium trioxide was prepared by dissolving 5.6 g (0.056 mole) of chromium trioxide in 8 ml of water, adding 86 g (0.088 mole) of concentrated sulfuric acid to the solution while cooling it in an ice bath and then diluting the mixture with 16 ml of water. This solution was then added dropwise over a period of 30 minutes to an acetone solution of 31.6 g (0.23 mole) of the resulting alcohol while the solution was maintained at a temperature below 5° C. and stirred. The mixture was stirred at a temperature below 20° C., and then the resulting reaction mixture was treated by addition thereto of sodium hydrogen sulfite to form two separate layers. The lower layer was extracted with petroleum ether, and the petroleum ether layer was then combined with the upper layer previously obtained. The combined layers were washed with alkali hydroxide and then with water, and were distilled after being dried over anhydrous magnesium sulfate, thereby affording a ketone (5-vinyl-2 or 3-norbornanone) having a boiling point of 47°–48° C./0.35 mmHg in a yield of 77%.

The resultant ketone was analyzed by vapor phase chromatography (column filler: Silicone SE-30; column dimensions: 90 m in length and 0.25 m in diameter; stainless steel; column temperature, 150° C.). The analysis revealed that the resultant ketone was a mixture of 5-vinyl-2-norbornanone and 5-vinyl-3-norbornanone in a ratio of the former to the latter of about 70:30. The subsequent acetal formation did not change the ratio of the position isomers.

ir (neat method):

A strong absorption peak at 1,750  $\text{cm}^{-1}$  (stretching vibration of  $>\text{C}=\text{O}$ ) appeared, and the stretching vibrations of  $\text{C}-\text{O}$  (1,000–1,110  $\text{cm}^{-1}$ ) and  $\text{O}-\text{H}$  of the alcohol ( $\sim 3,400 \text{ cm}^{-1}$ ) disappeared.

nmr:

4.0–4.6  $\tau$  (multiplet, 1H),  
4.8–5.2  $\tau$  (multiplet, 2H),  
7.0–8.6  $\tau$  (multiplet, 8H).

$n_D^{15}$ : 1.4930

Elemental Analysis (as  $\text{C}_9\text{H}_{12}\text{O}$ ):

	C(%)	H(%)
Calculated:	79.43	8.82
Found:	79.40	8.89

#### Preparation Example 2

Synthesis of 5-ethylidene-2 and 3-norbornanones 5-Ethylidene-2-norbornene, 36.0 g (0.300 mole) was dissolved in 250 ml of dry tetrahydrofuran, and 5.0 g (0.129 mole) of sodium borohydride was added thereto. Boron trifluoride, 14.0 ml (0.111 mole) ether complex was dropwise added over about 30 minutes to the solution, while it was cooled in an ice bath. The mixture was thereafter stirred at 10°–20° C. for about 2 hours. To the resulting reaction mixture which was cooled with ice were added 25.2 ml of water and 34.1 ml of 3 N sodium hydroxide aqueous solution, and then gradually 34.1 ml of a 30% hydrogen peroxide aqueous solution was dropwise added. The resultant reaction mixture was stirred at about 50° C. for 2 hours and poured into 100 ml of a benzene-ether mixture. The mixture was washed several times with small amounts of saturated salt aqueous solution. The separated organic layer was dried

over anhydrous magnesium sulfate, and the solvent was distilled off to afford residual materials which in turn were distilled under reduced pressure to given colorless 5-ethylidene-2 or 3-norbornanol (yield: 24.8 g, 60%, b.p., 60°–61° C./0.45 mmHg).

ir (neat method):

$\sim 3,300 \text{ cm}^{-1}$  (stretching vibration of  $\text{O}-\text{H}$ ),  
 $\sim 1,680 \text{ cm}^{-1}$  (stretching vibration of  $\text{C}=\text{C}$  of ethylidene group),  
1,060–1,080  $\text{cm}^{-1}$  (stretching vibration of  $\text{C}-\text{O}$  of the alcohol)

nmr ( $\text{CDCl}_3$ ):

4.5–5.0  $\tau$  (multiplet, 1H),  
6.0–6.3  $\tau$  (multiplet, 1H),  
6.7  $\tau$  (singlet, 1H),  
7.2  $\tau$  (broad singlet, 1H),  
7.5–7.7  $\tau$  (multiplet, 1H),  
8.4  $\tau$  (singlet, 3H),  
7.9–8.9  $\tau$  (multiplet, 6H).

Elemental Analysis (as  $\text{C}_9\text{H}_{14}\text{O}$ ):

	C(%)	H(%)
Calculated:	78.3	1.0
Found:	77.6	1.1

It was found from gas chromatography analysis that 95% of the resultant alcohol product was in the exo form, and 65% of the product was 5-ethylidene-2-norbornanol. No tricyclic-type compound was found at all.

A mixture of 5-ethylidene-2-norbornanol and 5-ethylidene-3-norbornanol, 5.0 g (0.036 mole) prepared above and 19.6 g (0.181 mole) of para-benzoquinone were dissolved in 160 ml of dry toluene.

Aluminum triisopropoxide, 3.7 g (0.018 mole) was gradually added at room temperature to the solution under stirring. After the reaction mixture was heated under reflux for 1 hour, 100 ml of sodium potassium tartarate saturated solution was added thereto and the mixture was extracted with a benzene-ether mixture. The extract was washed once with sodium hydrogen carbonate saturated solution and twice with water, and was distilled under reduced pressure after drying over anhydrous magnesium sulfate, leaving 4.2 g of 5-ethylidene-2 and 3-norbornanone (yield, 85%; b.p., 59°–60° C./1.8 mmHg).

ir (neat method):

1,760  $\text{cm}^{-1}$  (stretching vibration of  $>\text{C}=\text{O}$ ),  
 $\sim 1,685 \text{ cm}^{-1}$  (stretching vibration of  $\text{C}=\text{C}$  of ethylidene group).

The stretching vibration of  $\text{O}-\text{H}$  ( $\sim 3,400 \text{ cm}^{-1}$ ) was lost through oxidation.

nmr ( $\text{CDCl}_3$ ):

4.4–4.7  $\tau$  (multiplet, 0.6H),  
8.0–8.4  $\tau$  (multiplet, 8H),  
8.8–9.2  $\tau$  (quartet, 3H).

$n_D^{15}$ : 1.4804.

Elemental Analysis (as  $\text{C}_9\text{H}_{12}\text{O}$ ):

	C(%)	H(%)
Calculated:	79.41	8.82
Found:	79.05	8.60

Gas chromatography analysis revealed that 5-ethylidene-2-norbornanone predominated, of which the exo form amounted to 95%.

*This Page Blank (uspto)*

## EXAMPLE 1

## Synthesis of spiro[1,3-dioxolane-2,2' or 2,3'-(5'-vinylnorbornane)]

The ketone, 25 g (0.18 mole) prepared in Preparation Example 1 (5-vinyl-2 or 3-norbornanone), 14 g (0.22 mole) of ethylene glycol and a small amount of para-toluenesulfonic acid were added to 100 ml of benzene. The mixture was heated under reflux to remove the formed water by azeotropic distillation. After about 30 minutes, the reaction mixture was cooled to room temperature. The mixture was mixed with a small amount of anhydrous sodium carbonate and then stirred well. The resulting reaction mixture was washed with a small amount of water to remove most of the alkaline materials, and the benzene layer was dried over anhydrous magnesium sulfate. After benzene was distilled for removal, the residual materials were distilled under reduced pressure to give the acetal compound represented hereinabove as the title compound. The yield was 92% and the title compound was a colorless liquid which have green acid camphorous order.

Boiling point:

61°-62° C./0.7 mmHg.

$n_D^{23}$ :

1.4918.

ir (neat method):

3,050  $\text{cm}^{-1}$  (stretching vibration of C—H of the vinyl group),

1,630  $\text{cm}^{-1}$  (stretching vibration of C=C)

The stretching vibration of C=O (1,730  $\text{cm}^{-1}$ ) was lost by conversion into acetal.

nmr ( $\text{CDCl}_3$ ):

3.8-4.5  $\tau$  (sextet, 1H),

4.8-5.3  $\tau$  (multiplet, 2H),

6.1  $\tau$  (singlet, 4H),

7.2-8.7  $\tau$  (multiplet, 9H).

Elemental Analysis (as  $\text{C}_{11}\text{H}_{16}\text{O}_2$ )

	C(%)	H(%)
Calculated:	73.3	8.9
Found:	73.5	8.5

The resultant spiro [1,3-dioxolane-2,2' or 2,3'-(5'-vinylnorbornane)] was formulated in the following composition to provide a base perfume in muguet (lily of the valley) note. The product can also be used as a component for Eau de Cologne having narcissus, lily-of-the-valley, lily, lilac or orange flower note.

Phenylethyl alcohol	260 g
phenylacetic acid	25 g
Dimethylbenzyl carbinol	25 g
$\alpha$ -Ionone	75 g
Algerian jasmine absolute	10 g
Benzyl acetate	50 g
$\alpha$ -Amylcinnamic aldehyde	60 g
Citral	20 g
Aurantol	95 g
Heliotropin	45 g
Linalool	70 g
Vanillin	10 g
10% Indole ethanol solution	30 g
Methyl Jasmonate	40 g
Terpineol	150 g
Acetal prepared above	35 g
Total	1,000 g

## EXAMPLE 2

## Synthesis of spiro[4,5-dimethyl-1,3-dioxolane-2,2' or 2,3'-(5'-vinylnorbornane)]

The ketone prepared in Preparation Example 1 was converted into the corresponding acetal in the same manner as in Example 1 to give the title compound in a 78.7% yield.

Boiling point:

83°-84° C./1.5 mm Hg.

$n_D^{23}$ :

1.4741

ir (neat method):

3,052  $\text{cm}^{-1}$  (stretching vibration of C—H of vinyl group),

1,630  $\text{cm}^{-1}$  (stretching vibration of C=C),

The stretching vibration of  $>\text{C}=\text{O}$  (1,730  $\text{cm}^{-1}$ ) disappeared through conversion into acetal.

nmr ( $\text{CDCl}_3$ ):

3.5-4.6  $\tau$  (sextet, 1H),

4.8-5.3  $\tau$  (multiplet, 2H),

6.0-6.1  $\tau$  (quartet, 2H),

7.1-8.7  $\tau$  (multiplet, 9H),

8.8-9.0  $\tau$  (doublet, 6H).

Elemental Analysis (as  $\text{C}_{13}\text{H}_{20}\text{O}_2$ ):

	C(%)	H(%)
Calculated:	75.0	9.6
Found:	74.7	9.9

The resultant spiro[4,5-dimethyl-1,3-dioxolane-2,2' or 2,3'-(5'-vinylnorbornane)] was formulated in the following composition to provide a perfume in lavender note for use in soaps. The product can also be used in hair tonic for men by diluting it with refined alcohol.

English lavender oil	525 g
Bourbon bergamot oil	80 g
Indonesian bois de rose oil	100 g
Geranium oil	50 g
Rcmarin oil	50 g
Patchouli oil	25 g
Coumarin	40 g
Musk ketone	30 g
Heliotropin	50 g
Benzoic acid	25 g
Acetal prepared above	25 g
Total	1,000 g

## EXAMPLE 3

## Synthesis of spiro[1,3-dioxane-2,2' or 2,3'-(5'-vinylnorbornane)]

The ketone prepared in Preparation Example 1 was converted into the corresponding acetal with trimethylene glycol in the same manner as in Example 1 to give the title compound in a 79.7% yield.

Boiling point:

98°-99° C./2.0 mmHg.

$n_D^{24}$ :

1.4984.

ir (neat method):

3,050  $\text{cm}^{-1}$  (stretching vibration of C—H of vinyl group),

1,630  $\text{cm}^{-1}$  (stretching vibration of C=C),

The stretching vibration of  $>\text{C}=\text{O}$  (1,730  $\text{cm}^{-1}$ ) was lost in the actual conversion.

This Page Blank (uspto)

nmr (CDCl<sub>3</sub>):

- 3.7–4.4  $\tau$  (sextet, 1H),  
 4.8–5.2  $\tau$  (multiplet, 2H),  
 6.1–6.2  $\tau$  (triplet, 4H)  
 7.0–8.8  $\tau$  (multiplet, 11H).

Elemental Analysis (as C<sub>12</sub>H<sub>18</sub>O<sub>2</sub>):

	C(%)	H(%)
Calculated:	74.2	9.3
Found:	73.8	9.5

The spiro[1,3-dioxane-2,2' or 2,3'-(5'-vinylnorbornane)] prepared hereinabove as formulated in the following composition to provide a perfume in fougere notes. This compound can also be used as a base for oriental perfumes for women.

Madagascar terpeneless bergamot oil	100 g
Linalool	150 g
Mysore sandalwood oil	100 g
Coumarin	100 g
English orris oil	60 g
Vanillin	20 g
Musk ambrette	20 g
Linalyl acetate	70 g
Bulgarian rose absolute	50 g
Musk ketone	50 g
Acetal prepared hereinabove	170 g
Total	890 g

## EXAMPLE 4

Synthesis of spiro[5,5-dimethyl-1,3-dioxane-2,2' or 2,3'-(5'-vinylnorbornane)]

The ketone prepared in Preparation Example 1 was converted into the corresponding acetal with 2,2-dimethyl-1,3-propanediol in the same manner as in Example 1 to provide the title compound in a 75.8% yield.

Boiling point:

69°–70° C./0.25 mmHg,

 $n_D^{24}$ :

1.4841

ir (neat method):

3,060 cm<sup>-1</sup> (stretching vibration of C—H of vinyl group),1,625 cm<sup>-1</sup> (stretching vibration of C=C),The stretching vibration of >C=O (1,730 cm<sup>-1</sup>) was lost in the acetal conversion.nmr (CDCl<sub>3</sub>):

- 3.7–4.5  $\tau$  (sextet, 1H),  
 4.7–5.2  $\tau$  (multiplex, 2H),  
 6.1  $\tau$  (singlet, 4H),  
 7.2–8.7  $\tau$  (multiplet, 9H),  
 9.0  $\tau$  (singlet, 6H).

Elemental Analysis (as C<sub>14</sub>H<sub>22</sub>O<sub>2</sub>):

	C(%)	H(%)
Calculated:	75.7	9.9
Found:	75.9	10.1

The spiro[5,5-dimethyl-1,3-dioxane-2,2' or 2,3'-(5'-vinylnorbornane)] prepared hereinabove was formulated in the following composition to provide a chypres base perfume. This base perfume can be used as a component of modern chypre notes for women's cosmetics.

Madagascar terpeneless bergamot oil	200 g
Fench rose absolute	200 g
Methyl anthranilate	50 g
Vanillin	70 g
Heliotropin	50 g
Phenylethyl alcohol	100 g
Irone	30 g
Acetal prepared hereinabove	300 g
Total	1,000 g

## EXAMPLE 5

Synthesis of spiro[4-methyl-1,3-dioxane-2,2' or 2,3'-(5'-vinylnorbornane)]

The ketone prepared in Preparation Example 1 was converted into the corresponding acetal with 1,3-butanediol in the same manner as in Example 1 to provide the title compound in a 70.4% yield.

Boiling point: 82–83° C./0.80 mmHg

 $n_D^{25}$ : 1.4887

ir (neat method):

3,050 cm<sup>-1</sup> (stretching vibration of C—H of vinyl group),1,625 cm<sup>-1</sup> (stretching vibration of C=C)The stretching vibration of >C=O (1,730 cm<sup>-1</sup>) was lost in the acetal conversion.nmr (CDCl<sub>3</sub>):

- 3.8–4.5  $\tau$  (sextet, 1H),  
 4.7–5.2  $\tau$  (multiplet, 2H),  
 6.1–6.3  $\tau$  (multiplex, 3H),  
 7.1–8.6  $\tau$  (multiplet, 11H),  
 8.9  $\tau$  (doublet, 3H).

Elemental Analysis (as C<sub>13</sub>H<sub>20</sub>O<sub>2</sub>):

	C(%)	H(%)
Calculated:	75.0	9.6
Found:	74.6	9.5

The spiro[4-methyl-1,3-dioxane-2,2' or 2,3'-(5'-vinylnorbornane)] prepared hereinabove was formulated in the following composition to provide a perfume in Oriental rose notes. This perfume can be used conveniently for various uses as a formulation base in the rose series.

Perfume prepared in Example 1	150 g
$\alpha$ -Ionone	25 g
Bulgarian rose oil	50 g
Phenyl acetate	5 g
Bourbon geranium oil	50 g
Phenyl ethyl alcohol	120 g
Rhodinol	250 g
Mysore sandalwood oil	10 g
Musk Tincture	10 g
Mixed artificial musk oils	100 g
Lavol, (3,6-dimethylocton-3-01)	30 g
Acetal prepared hereinabove	100 g
Total	900 g

## EXAMPLE 6

Synthesis of spiro [5,5-diethyl-1,3-dioxane-2,2' or 2,3'-(5'-vinylnorbornane)]

The ketone prepared in Preparation Example 1 was converted into the corresponding acetal with 2,2-diethyl-3-propanediol in the same manner as in Example 1 to provide the title compound in a 78.0% yield.

**This Page Blank (uspto)**

Boiling point:

77°–78° C./0.20 mmHg,

$n_D^{24}$ :

1.4910,

ir (neat method):

3,050  $\text{cm}^{-1}$  (stretching vibration of C—H of vinyl group),

1,630  $\text{cm}^{-1}$  (stretching vibration of C=C),

The stretching vibration of  $>\text{C}=\text{O}$  (1,730  $\text{cm}^{-1}$ ) was lost in the acetal conversion.

nmr ( $\text{CDCl}_3$ ):

3.8–4.5  $\tau$  (sextet, 1H),

4.8–5.2  $\tau$  (multiplet, 2H),

6.1  $\tau$  (singlet, 4H),

7.2–8.7  $\tau$  (multiplet, 13H)

8.9–9.1  $\tau$  (triplet, 6H).

Elemental Analysis (as  $\text{C}_{16}\text{H}_{26}\text{O}_2$ ):

	C(%)	H(%)
Calculated:	76.8	10.4
Found:	76.4	10.3

The spiro[5,5-diethyl-1,3-dioxane-2,2' or 2,3'-(5'-vinylnorbornane)] prepared hereinabove was formulated in the following composition to provide a perfume for soaps in violet note. This perfume is also useful as a base for rose-violet type formulated cosmetics.

$\alpha$ -Ionone	300 g
Methylionone	100 g
$\alpha$ -Hexylcinnami aldehyde	20 g
Benzyl acetate	30 g
Benzyl alcohol	100 g
Heliotropin	100 g
French bergamot oil	125 g
Moroccan rose absolute	10 g
Phenylethyl alcohol	140 g
Leaf alcohol, (cis-3-hexenol)	5 g
Acetal prepared hereinabove	70 g
Total	1,000 g

#### EXAMPLE 7

Synthesis of spiro[4,5-tetramethylene-1,3-dioxolane-2,2' or 2,3'-(5'-vinylnorbornane)]

The ketone prepared in Preparation Example 1 was converted into the corresponding acetal with 1, 2-cyclohexanediol in the same manner as in Example 1 to provide the title compound in a 64.1% yield.

Boiling point: 92°–94° C./0.02 mmHg,

$n_D^{24}$ :

1.5028,

ir (neat method):

3,050  $\text{cm}^{-1}$  (stretching vibration of C—H of vinyl group),

1,625  $\text{cm}^{-1}$  (stretching vibration of C=C),

The stretching vibration of  $>\text{C}=\text{O}$  (1,730  $\text{cm}^{-1}$ ) was lost in the acetal conversion.

nmr ( $\text{CDCl}_3$ ):

3.7–4.3  $\tau$  (sextet, 1H),

4.7–5.3  $\tau$  (multiplet, 2H),

5.9–6.0  $\tau$  (triplet, 2H),

7.2–8.9  $\tau$  (multiplet, 17H).

Elemental Analysis (as  $\text{C}_{15}\text{H}_{22}\text{O}_2$ ):

	C(%)	H(%)
Calculated	76.9	9.4
Found:	77.2	9.3

The spiro[4,5-tetramethylene-1,3-dioxolane-2,2' or 2,3'-(5'-vinylnorbornane)] was formulated in the following composition to provide a perfume in a kind of orchard cattleya note.

Hydroxycitronellal	150 g
Terpineol	125 g
Madagascar ylang-ylang oil	100 g
Phenylethyl alcohol	70 g
Jasmone	20 g
Linalool	40 g
$\alpha$ -Amylcinnamic aldehyde	20 g
Methylnonyl acetaldehyde	10 g
Isobutyl asicylate	150 g
Benzyl salicylate	25 g
Ethylvanillin	10 g
Heliotropin	20 g
Synthetic macro-ring ketone, (Exaltone)	20 g
Coumarin	40 g
$\alpha$ -Ionone	50 g
Zanzibar bergamot oil	100 g
Acetal prepared hereinabove	50 g
Total	1,000 g

This perfume can be used as an attractive deodorant for use in room by mixing it with an aqueous gel of sodium polyacrylate. It can also be employed as a disinfectant-odorant for use in detergents by mixing it with methyl violet, a surfactant and polyethylene oxide to thereby shape a desired form.

#### EXAMPLE 8

Synthesis of spiro[1,3-dioxolane-2,2' or 2,3'-(5'-ethylidene norbornane)]

The ketone prepared in Preparation Example 2 was converted into the corresponding acetal with ethylene glycol in the same manner as in Example 1 to provide the title compound, i.e., 5-ethylidenenorbornanone ethyleneacetal (2.1 g; yield, 63.5%; b.p., 61–62°/0.30 mmHg).

ir (neat method):

~1,690  $\text{cm}^{-1}$  (stretching vibration of C=C of ethylidene group),

The stretching vibration of C=O (~1,750  $\text{cm}^{-1}$ ) was lost in the acetal conversion.

nmr ( $\text{CDCl}_3$ ):

4.6–5.0  $\tau$  (multiplet, 1H)

6.2  $\tau$  (singlet, 4H)

7.5  $\tau$  (broad singlet, 1H)

7.6–7.8  $\tau$  (multiplet 1H)

8.4  $\tau$  (singlet, 3H)

7.9–9.0  $\tau$  (multiplet, 6H)

Elemental Analysis (as  $\text{C}_{11}\text{H}_{16}\text{O}_2$ ):

	C(%)	H(%)
Calculated:	73.3	8.9
Found:	73.8	8.7

The spiro[1,3-dioxolane-2,2' and 2,3' (5'-ethylidenenorbornane)] was formulated in the following composition to provide a perfume composition useful as a base for a lily fragrance. This composition can be used as a perfume for soaps.

This Page Blank (uspia)

phenylethyl alcohol	10.9 g
Benzyl alcohol	10.9 g
Dimethylbenzyl carbinol	3.3 g
$\beta$ -Ionone	6.6 g
Benzyl acetate	5.5 g
$\alpha$ -Amylcinnamic aldehyde	6.6 g
Citral	1.6 g
Aurantol	4.4 g
Heliotropin	2.2 g
Linalool	25.0 g
Musk xylene	3.3 g
10% Indole methanol solution	3.3 g
Methyl jasmonate	4.4 g
Terpineol	8.2 g
Acetal prepared hereinabove	3.8 g
Total	100 g

## EXAMPLE 9

## Synthesis of spiro[4,5-dimethyl-1,3-dioxolane-2,2' and 2,3'-(5'-ethylidene norbornane)]

The ketone (5-ethylidene-2 and 3-norbornanone) prepared in Preparation Example 2 was converted into the corresponding acetal with 2,3-butanediol in the same manner as in Example 1 to provide the title compound in a 70.0% yield.

b.p.: 68°-70° C./0.6 mmHg,

$n_D^{23}$ :

1.4692

ir (neat method):

1,640  $\text{cm}^{-1}$  (stretching vibration of C=C of ethylidene group)

The stretching vibration of  $>\text{C}=\text{O}$  (1,730  $\text{cm}^{-1}$ ) was lost by the acetal formation

nmr ( $\text{CDCl}_3$ ):

4.6-5.1  $\tau$  (multiplet, 1H)

6.0-6.1  $\tau$  (quartet, 2H)

7.4-8.7  $\tau$  (multiplet, 8H)

8.4  $\tau$  (singlet, 3H)

8.8-9.0  $\tau$  (doublet, 6H)

Elemental Analysis (as  $\text{C}_{13}\text{H}_{20}\text{O}_2$ ):

	C(%)	H(%)
Calculated:	75.0	9.6
Found:	74.5	9.8

The spiro[4,5-dimethyl-1,3-dioxolane-2,2' and 2,3'-(5'-ethylidenenorbornane)] was formulated in the following composition to provide a perfume in lavender note for use in soaps. This can also be used as a base perfume for men's cologne.

Lavender oil	47.2 g
Bergamot oil	9.4 g
Bois de rose oil	11.8 g
Geranium oil	5.9 g
Petitgrain oil	2.9 g
Patchouli oil	2.9 g
Coumarin oil	4.7 g
Musk ketone	3.5 g
Heliotropin	5.9 g
Vanillin	2.9 g
Acetal prepared hereinabove	2.9 g
Total	100 g

## EXAMPLE 10

## Synthesis of spiro[1,3-dioxane-2,2' and 2,3'-(5'-ethylidenenorbornane)]

The ketone (5-ethylidene-2 and 3-norbornanone) prepared in Preparation Example 2 was converted into the corresponding acetal with trimethylene glycol in the same manner as in Example 1 to provide the title compound in an 80% yield.

b.p.:

72° C./0.40 mmHg

$n_D^{24}$ :

1.4831

ir (neat method):

1,640  $\text{cm}^{-1}$  (stretching vibration of C=C of ethylidene group)

The stretching vibration of  $\text{C}=\text{O}$  (1,730  $\text{cm}^{-1}$ ) was lost in the acetal conversion.

nmr ( $\text{CDCl}_3$ ):

4.5-5.0  $\tau$  (multiplet, 1H),

6.1-6.2  $\tau$  (triplet, 4H),

8.4  $\tau$  (singlet, 3H),

7.2-8.8  $\tau$  (multiplet, 10H).

Elemental Analysis (as  $\text{C}_{12}\text{H}_{18}\text{O}_2$ ):

	C(%)	H(%)
Calculated	74.2	9.3
Found	73.8	9.5

The spiro[1,3-dioxane-2,2' and 2,3'-(5'-ethylidenenorbornane)] prepared hereinabove was formulated in the following composition to provide a perfume in floral-fougere note. This can be used as a base for fragrant gel perfumes for use in rooms.

Bergamot oil	10.0 g
Phenylethyl alcohol	11.0 g
Linalool	11.0 g
Linalyl acetate	4.0 g
Sandalwood oil	10.0 g
Heliotropin	5.0 g
Coumarin	5.0 g
Orris oil	6.0 g
Vanillin	2.0 g
Musk ambrette	2.0 g
Linalyl benzoate	7.0 g
Rose absolute	5.0 g
Macro-ring ketone (TMII-SP, 5-cyclohexadecenone)	5.0 g
Acetal prepared hereinabove	17.0 g
Total	100 g

## EXAMPLE 11

## Synthesis of spiro[5,5-dimethyl-1,3-dioxane-2,2' and 2,3'-(5'-ethylidenenorbornane)]

The ketone (5-ethylidene-2 and 3-norbornanone) prepared in Preparation Example 2 was converted into the corresponding acetal with 2,2-dimethyl-1,3-propanediol in the same manner as in Example 1 to provide the title compound in a 65.5% yield.

b.p.:

108°-109° C./3.0 mmHg,

$n_D^{24}$ :

1.4755,

ir (neat method):

1,635  $\text{cm}^{-1}$  (stretching vibration of C=C of ethylidene group)

This Page Blank (uspto;

The stretching vibration of  $>C=O$  ( $1,730\text{ cm}^{-1}$ ) was lost by the acetal formation.

nmr ( $CDCl_3$ ):

4.5–5.1  $\tau$  (multiplet, 1H),

6.1  $\tau$  (singlet, 4H),

8.3  $\tau$  (singlet, 3H)

7.3–8.7  $\tau$  (multiplet, 8H),

9.0  $\tau$  (singlet, 6H),

Elemental Analysis (as  $C_{14}H_{22}O_2$ ):

	C(%)	H(%)
Calculated:	75.7	9.9
Found:	75.8	10.0

The spiro[5,5-dimethyl-1,3-dioxane-2,2' and 2,3'-(5'-ethylidenenorbornane)] prepared hereinabove was formulated in the following composition to provide a cypress base aerosol pack perfume of chypre type eau de toilette.

Bergamot oil	20.8 g
Rose absolute	9.4 g
Zdrabetz oil	1.0 g
Methyl anthranilate	5.2 g
Terpineol	7.3 g
Vanillin	7.3 g
Ambrette	3.1 g
Heliotropin	5.2 g
Methylionone	1.0 g
Phenylethyl alcohol	7.3 g
Phenylethyl acetate	3.1 g
Irone	3.1 g
Acetal prepared hereinabove	26.2 g
Total	100 g

#### EXAMPLE 12

Synthesis of spiro[4-methyl-1,3-dioxane-2,2' and 2,3'-(5'-ethylidenenorbornane)]

The ketone(5-ethylidene-2 and 3-norbornanone) prepared in Preparation Example 2 was converted into the corresponding acetal with 1,3-butanediol in the same manner as in Example 1 to provide the title compound in a 70% yield.

b.p.:

82°–83° C./0.65 mmHg

$n_D^{24}$ :

1.4898

ir (neat method):

1,635  $\text{cm}^{-1}$  (stretching vibration of  $C=C$  of ethylidene group),

The stretching vibration of  $>C=O$  ( $1,730\text{ cm}^{-1}$ ) was lost by the acetal formation.

nmr ( $CDCl_3$ ):

4.6–5.0  $\tau$  (multiplet, 1H),

6.1–6.3  $\tau$  (multiplet, 3H),

8.5  $\tau$  (singlet, 3H),

7.3–8.8  $\tau$  (multiplet, 10H), 8.9  $\tau$  (doublet, 3H).

Elemental Analysis (as  $C_{13}H_{20}O_2$ ):

	C(%)	H(%)
Calculated:	75.0	9.6
Found:	74.7	9.8

The spiro[4-methyl-1,3-dioxane-2,2' and 2,3'-(5'-ethylidenenorbornane)] prepared hereinabove was formulated in the following composition to provide a perfume

in oriental rose notes. This perfume can be conveniently used for various purposes as a roseous base.

Perfume according to the formulation of

Example 1	10.6 g
Methylionone	2.1 g
Rose absolute	3.2 g
Zdrabetz oil	2.1 g
Phenyl acetic acid	0.5 g
Geranium oil	6.4 g
Phenylethyl alcohol	16.0 g
Aurantol	2.1 g
Rhodinol	26.6 g
Dimethylbenzyl carbinol	3.2 g
Sandalwood oil	1.1 g
Tonquin musk tincture	1.1 g
Mixed artificial must oil	10.1 g
Benzyl salicylate	4.3 g
Acetal prepared hereinabove	10.6 g
Total	100 g

#### EXAMPLE 13

Synthesis of spiro[5,5-diethyl-1,3-dioxane-2,2' and 2,3'-(5'-ethylidenenorbornane)]

The ketone (5-ethylidene-2 and 3-norbornanone) prepared in Preparation Example 2 was converted into the corresponding acetal with 2,2-diethyl-1,3-propanediol in the same manner as in Example 1 to provide the title compound in a 68% yield.

b.p.:

75°–77° C./0.20 mmHg,

$n_D^{24}$ :

1.4835

ir (neat method):

1,640  $\text{cm}^{-1}$  (stretching vibration of  $C=C$  of ethylidene group), The stretching vibration of  $>C=O$  ( $1,730\text{ cm}^{-1}$ ) was lost by the acetal formation.

nmr ( $CDCl_3$ ):

4.5–5.0  $\tau$  (multiplet, 1H),

6.1  $\tau$  (singlet, 4H),

8.4  $\tau$  (singlet, 3H),

7.3–8.9  $\tau$  (multiplet, 12H),

8.9–9.1  $\tau$  (triplet, 6H).

Elemental Analysis (as  $C_{16}H_{26}O_2$ ):

	C(%)	H(%)
Calculated:	76.8	10.4
Found:	76.2	10.1

The spiro[5,5-diethyl-1,3-dioxane-2,2' and 2,3'-(5'-ethylidenenorbornane)] was formulated into the following composition to provide a perfume for a detergent with violet notes.

$\alpha$ -Ionone	27.5 g
Methylionone	9.2 g
$\alpha$ -Hexylcinnamic aldehyde	1.8 g
Dihydrojasmine acid methyl ester	1.8 g
Benzyl alcohol	9.2 g
Heliotropin	9.2 g
Bergamot oil	11.5 g
Benzyl salicylate	4.6 g
Rose absolute	0.9 g
Phenylethyl alcohol	12.8 g
Leaf alcohol, (cis-3-hexenol)	0.5 g
Acetal prepared hereinabove	11.0 g
Total	100 g

This Page Blank (uspto)

## EXAMPLE 14

## Synthesis of spiro[4.5-tetramethylene-1,3-dioxolane-2,2' and 2,3'-(5'-ethylidenenorbornane)]

The ketone (5-ethylidene-2 and 3-norbornanone) prepared in Preparation Example 2 was converted into the corresponding acetal with 1,2-cyclohexanediol in the same manner as in Example 1 to provide the title compound in a 60.5% yield.

b.p.: 92°-94° C./0.35 mmHg,

$n_D^{24}$ : 1.4950,

ir (neat method):

1,635  $\text{cm}^{-1}$  (stretching vibration of C=C of ethylidene group),

The stretching vibration of  $>\text{C}=\text{O}$  (1,730  $\text{cm}^{-1}$ ) was lost by the acetal formation.

nmr ( $\text{CDCl}_3$ ):

4.6-5.0  $\tau$  (multiplet, 1H),

5.9-6.0  $\tau$  (triplet, 2H),

8.3  $\tau$  (singlet, 3H),

7.3-8.9  $\tau$  (multiplet, 16H).

Elemental Analysis (as  $\text{C}_{15}\text{H}_{22}\text{O}_2$ ):

	C(%)	H(%)
Calculated:	76.9	9.4
Found:	77.1	9.2

The spiro[4.5-tetramethylene-1,3-dioxolane-2,2' and 2,3'-(5'-ethylidenenorbornane)] prepared hereinabove was formulated into the following composition to provide a floral bouquet perfume which may be used as a component for a deodorant, malodour masking agent, or as an agent for imparting a fragrance to household products.

Hydroxycitronellal	10.3 g
Terpineol	12.8 g
Ylang-ylang oil	10.3 g
Jasmone	2.1 g
Phenylethyl alcohol	10.3 g
Linalool	6.2 g
$\alpha$ -Amylcinnamic aldehyde	3.1 g
Methylnonyl acetaldehyde	1.0 g
Isoamyl salicylate	10.3 g
Benzyl salicylate	2.6 g
Lily aldehyde	1.0 g
Ethylvanillin	1.0 g
Heliotropin	2.1 g
Synthetic macro-ring ketone, (5-cyclohexadecenone)	2.1 g
Coumarin	4.1 g
$\alpha$ -Ionone	5.2 g
Bergamot oil	10.3 g
Acetal prepared hereinabove	5.2 g
Total	100 g

## EXAMPLE 15

## Synthesis of spiro[1,3-dioxolane-2,2' and 2,3'-(5'-isopropylidenenorbornane)]

5-Isopropylidene-2-norbornene was treated in the same manner as in Preparation Example 2 to give 5-isopropylidene-2 and 3-norbornanol which was oxidized to the ketone. The ketone was converted into the corresponding acetal with ethylene glycol in the same manner as in Example 1 to provide the title compound in a 65% yield.

b.p.:

65°-67° C./0.60 mmHg,

$n_D^{24}$ :

1.4820

ir (neat method):

1,665  $\text{cm}^{-1}$  (weak absorption, stretching vibration of C=C of isopropylidene group) The stretching vibration of  $>\text{C}=\text{O}$  (1,730  $\text{cm}^{-1}$ ) was lost by the acetal formation.

nmr ( $\text{CDCl}_3$ ):

6.1  $\tau$  (singlet, 4H),

7.4  $\tau$  (broad singlet, 1H),

8.3  $\tau$  (singlet, 3H),

8.4  $\tau$  (singlet, 3H),

7.9-8.8  $\tau$  (multiplet, 7H),

Elemental Analysis (as  $\text{C}_{12}\text{H}_{18}\text{O}_2$ ):

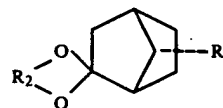
	C(%)	H(%)
Calculated:	74.2	9.3
Found:	73.5	9.5

The spiro[1,3-dioxolane-2,2' and 2,3'-(5'-isopropylidenenorbornane)] prepared hereinabove was formulated in the following composition to provide a floral perfume composition in lavender fougere note for use in soaps.

Lavender oil	17.9 g
Geranium oil	7.1 g
Oak moss resinoid	3.6 g
$\alpha$ -Ionone	4.4 g
Coumarin	5.4 g
Patchouli oil	4.5 g
Cedarwood oil	13.4 g
Sandalwood oil	3.6 g
Vetiver oil	0.9 g
Terpinyl acetate	11.6 g
Benzyl salicylate	8.0 g
Rhodinol	8.9 g
Musk ambrette	4.5 g
Labdanum resinoid	1.8 g
Acetal prepared hereinabove	4.4 g
Total	100 g

What is claimed is:

1. A compound represented by the general formula:



(I)

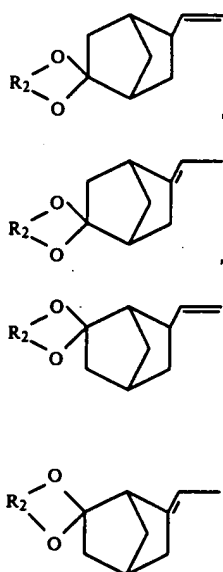
(wherein  $\text{R}_1$  is an alkenyl group having 2 or 3 carbon atoms or an alkylidene group having 1 to 3 carbon atoms and  $\text{R}_2$  is the saturated hydrocarbon group having 2 to 7 carbon atoms, with a dotted line between the two carbon atoms indicating a single bond when  $\text{R}_1$  is an alkenyl group and a double bond when  $\text{R}_1$  is alkylidene group).

2. The compound according to claim 1, wherein the compound is represented by the general formula (II)-1, (II)-2, (III)-1 or (III)-2:

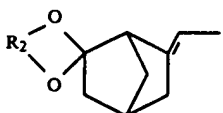
This Page Blank (uspto)

This Page Blank (uspto)

This Page Blank (uspto)



or



(wherein  $R_2$  is a saturated hydrocarbon group having 2 to 7 carbon atoms).

3. The compound according to claim 2, wherein the compound is spiro[1,3-dioxolane-2,2' or 2,3'-(5'-vinyl-norbornane)].

4. The compound according to claim 2, wherein the compound is spiro[4,5-dimethyl-1,3-dioxolane-2,2' or 2,3'-(5'-vinylnorbornane)].

5. The compound according to claim 2, wherein the compound is spiro[1,3-dioxane-2,2' or 2,3'-(5'-vinylnorbornane)].

6. The compound according to claim 2, wherein the compound is spiro[5,5-dimethyl-1,3-dioxane-2,2' or 2,3'-(5'-vinylnorbornane)].

7. The compound according to claim 2, wherein the compound is spiro[4-methyl-1,3-dioxane-2,2' or 2,3'-(5'-vinylnorbornane)].

8. The Compound according to claim 2, wherein the compound is spiro[5,5-diethyl-1,3-dioxane-2,2' or 2,3'-(5'-vinylnorbornane)].

9. The compound according to claim 2, wherein the compound is spiro[4,5-tetramethylene-1,3-dioxolane-2,2' or 2,3'-(5'-vinylnorbornane)].

10. The compound according to claim 2, wherein the compound is spiro[1,3-dioxolane-2,2' or 2,3'-(5'-ethylidenenorbornane)].

11. The compound according to claim 2, wherein the compound is spiro[4,5-dimethyl-1,3-dioxolane-2,2' or 2,3'-(5'-ethylidenenorbornane)].

12. The compound according to claim 2, wherein the compound is spiro[1,3-dioxane-2,2' or 2,3'-(5'-ethylidenenorbornane)].

13. The compound according to claim 2, wherein the compound is spiro[5,5-dimethyl-1,3-dioxane-2,2' or 2,3'-(5'-ethylidenenorbornane)].

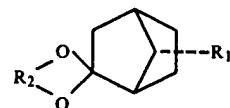
14. The compound according to claim 2, wherein the compound is spiro[4-methyl-1,3-dioxane-2,2' or 2,3'-(5'-ethylidenenorbornane)].

15. The compound according to claim 2, wherein the compound is spiro[5,5-diethyl-1,3-dioxane-2,2' or 2,3'-(5'-ethylidenenorbornane)].

16. The compound according to claim 2, wherein the compound is spiro[4,5-tetramethylene-1,3-dioxolane-2,2' or 2,3'-(5'-ethylidenenorbornane)].

17. A perfume composition containing as a perfume active constituent a compound of the general formula (I):

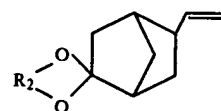
(III)-2 20



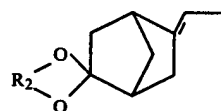
(I)

(wherein  $R_1$  is an alkenyl group having 2 or 3 carbon atoms or an alkylidene group having 1 to 3 carbon atoms and  $R_2$  is a saturated hydrocarbon group having 2 to 7 carbon atoms, with the dotted line between the two carbon atoms indicating a single bond when  $R_1$  is an alkenyl group and a double bond when  $R_1$  is an alkylidene group and a conventional adjuvant).

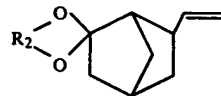
18. The perfume composition according to claim 17, wherein the compound is represented by general formula (II)-1, (II)-2, (III)-1 or (III)-2:



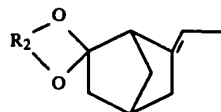
(II)-1



(II)-2



(III)-1



(III)-2

(wherein  $R_2$  is a saturated hydrocarbon group having 2 to 7 carbon atoms).

\* \* \* \* \*

60

65

This Page Blank (u5...

**United States Patent** [19]  
**Giraudi**

[11] **Patent Number:** **4,774,225**

[45] **Date of Patent:** **Sep. 27, 1988**

[54] **ODORANTS**

[75] **Inventor:** **Edouard Giraudi, La Roquette sur  
Siagne, France**

[73] **Assignee:** **Societe Anonyme Roure Bertrand  
Dupont, Argenteuil, France**

[21] **Appl. No.:** **114,785**

[22] **Filed:** **Oct. 30, 1987**

[30] **Foreign Application Priority Data**

Nov. 3, 1986 [EP] **European Pat. Off.** ..... 86.810497.7

[51] **Int. Cl.<sup>4</sup>** ..... **C07D 319/08; A61K 7/46**

[52] **U.S. Cl.** ..... **512/9; 549/336;  
568/831**

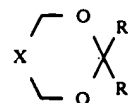
[58] **Field of Search** ..... **549/336; 512/9**

*Primary Examiner*—Norma S. Milestone

*Attorney, Agent, or Firm*—Sidney Wallenstein

[57] **ABSTRACT**

The invention relates to novel odorant substances. These are compounds of the formula



wherein R and R<sup>1</sup> are H, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>, C<sub>3</sub>H<sub>7</sub> or CH(CH<sub>3</sub>)<sub>2</sub> and the sum of the carbon atoms in R and R<sup>1</sup> does not exceed 6, and X is caran-yliden (2,2) or caran-yliden (4,4).

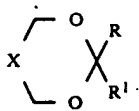
The invention relates also to the preparation of these novel substances and to odorant compositions containing these substances.

**8 Claims, No Drawings**

This Page Blank (usp.

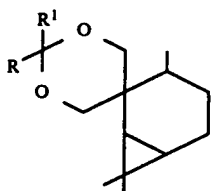
## ODORANTS

The invention is concerned with novel odorant substances. These are the compounds of the formula

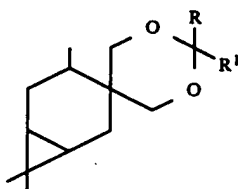


wherein R and R' are H, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>, C<sub>3</sub>H<sub>7</sub> or CH(CH<sub>3</sub>)<sub>2</sub> and the sum of the carbon atoms in R and R' does not exceed 6, and X is caran-yliden (2,2) or caran-yliden (4,4).

Formula I encompasses thus the compounds of formulae



and



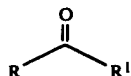
The compounds I have particular organoleptic properties, on the basis of which they are excellently suited as odorant substances.

The invention is accordingly also concerned with the use of the compounds I as odorant substances and odorant substance compositions containing compounds I.

2,2,3',7',7'-pentamethyl-spiro[1,3-dioxane-5,2'-norcaran] is the preferred compound I. Its odor characteristics can be described as follows: amber, woody (of most interesting complexity), recalling the odour of the fruits of eucalyptus in a very early green stage.

Further interesting compounds I are: 2,3',7',7'-tetramethyl-spiro[1,3-dioxane-5,2'-norcaran], 3',7',7'-trimethyl-2-ethyl-spiro[1,3-dioxane-5,2'-norcaran], 2,3',7',7'-tetramethyl-2-ethyl-spiro[1,3-dioxane-5,2'-norcaran], 3',7',7'-trimethyl-2,2-diethyl-spiro[1,3-dioxane-5,2'-norcaran] and 3',7',7'-trimethyl-spiro[1,3-dioxane-5,2'-norcaran].

The invention is also concerned with a process for the manufacture of the compounds I. This process comprises reacting 2- or 4-[bis-(hydroxymethyl)]caran with a carbonyl compound of the general formula



wherein R and R' are as above.

The manufacture of the compounds I is conveniently effected using methods described in the literature, such as acid-catalysed acetalisation or ketalisation, or, trans-

acetalisation or trans-ketalisation, e.g. by using an acetal or ketal of a low boiling compound II, see e.g.

—Frans A. J. Meskens, *Synthesis* (1981), 501 seq.

—M. Delmas, A. Gaset, *Informations Chimie* No. 232, (December 1982), 151-158.

As acidic catalysts there can be used the substances which are usually used for acetalisations or ketalisations; for example, mineral acids such as hydrochloric acid or sulphuric acid, phosphoric acid and perchloric acid, etc., strong organic acids such as trichloroacetic acid or p-toluenesulphonic acid, (PTSOH) etc. and Lewis acids such as, for example, boron trifluoride, etc.

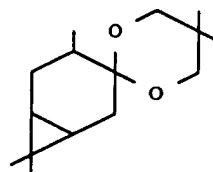
The reaction is suitably effected at room temperature or slightly elevated temperatures, if necessary in the presence of a solvent.

As solvents, there can be used for example, aromatic and saturated aliphatic hydrocarbons (e.g. benzene, toluene or n-pentane).

As pointed out above, the invention is also concerned with the use of the compounds I as odorant substances.

The dioxanes in accordance with the invention are all distinguished by woody and amber notes, exhibiting, in particular, flowery green side notes. Worth of mentioning are their odorous power and the tenacity. They are either colorless or slightly colored, readily accessible, the individual batches are constant in odor, non-irritant, stable and convenient to handle.

Thus, the novel compounds I are organoleptically totally different from the structurally related dioxane of the formula



as discussed on the "Colloque sur la chimie des terpènes", in Grasse, France, April 24-25, 1986.

This latter compound can be described as green, herbaceous with balsamous and resinous side notes and which compound did, due to its simple and common organoleptic aspect, not attract the interest of the perfumers at all.

The compounds I combines with numerous known odorant substance ingredients of natural or synthetic origin, whereby the range of the natural raw substances can embrace not only readily volatile but also semi-volatile and difficulty-volatile components, and that of the synthetics can embrace representatives from practically all classes of substances, as is evident from the following compilation:

Natural products, such as tree moss absolute, basil oil, agrumen oils (such as begamot oil, mandarin oil etc.), palmarosa oil, patchouli oil, petitgrain oil, wormwood oil, lavender oil, geranium oil, clove oil

alcohols, such as farnesol, geraniol, linalool, nerol, phenylethyl alcohol, rhodinol, cinnamic alcohol, aldehydes, such as citral, Helional®, α-hexylcinnamaldehyde, hydroxycitronellal, Lilial® (p-tert. butyl-α-methyl-dihydrocinnamaldehyde), methyl-nonylacetaldehyde,

This Page Blank (uspto)

ketones, such as allylionone,  $\alpha$ -ionone,  $\beta$ -ionone, isoraldein (isomethyl- $\alpha$ -ionone), methylionone, esters, such as allyl phenoxyacetate, benzyl salicylate, cinnamyl propionate, citronellyl acetate, benzyl acetate, citronellyl ethoxalate (citronellyl-O-CO-CO-OC<sub>2</sub>H<sub>5</sub>), decyl acetate, dimethylbenzylcarbinyl acetate, dimethylbenzylcarbinyl butyrate, ethyl acetoacetate, ethyl acetylacetate, hexenyl isobutyrate, linalyl acetate, methyl dihydrojasmonate, styrallyl acetate, vetiveryl acetate, lactones, such as  $\gamma$ -undecalactone,

various components often used in perfumery, such as musk ketone, indole, methyleugenol, Vertofix® (acetylated cedarwood oil), Képhalis® (1-ethoxy-4(1'-ethoxy-vinyl)-3,3,5,5-tetramethyl-cyclohexene/4(1'-ethoxy-vinyl)-3,3,5,5-tetramethyl-cyclohexanone, Argéolène® (Schiffbase of hydroxycitronellal and methyl anthranilate), etc.

Worthy of note is, further, the manner in which the compounds I rounds-off and harmonizes the olfactory notes of known compositions without, however, dominating in an unpleasant manner. The dioxanes can be used in a great variety of odorant compositions, e.g. in compositions of the following types:

oriental chypre, modern fougère, green tobacco, floral chypre, fresh fougère, floral sweet citrus, woody animal, oriental, floral fruity, floral aldehyde, leather, spicy, green, woody amber, musk, tobacco, etc.

The compounds of formula I (or its mixtures) can be used in wide limits which can extend in compositions, for example, from 0.1 (detergents)-5% (alcoholic solutions). It will be appreciated, however, that these values are not limiting values, as the experienced perfumer can also achieve effects with even lower concentrations or can synthesize novel complexes with even higher amounts. The preferred concentrations range between 0.2 and 2%. The compositions manufactured with I can be used for all kinds of perfumed consumer goods (eau de cologne, eau de toilette, extracts, lotions, creams, shampoos, soaps, salves, powders, toothpastes, mouth washes, deodorants, detergents, tobacco, etc.).

The compounds I can accordingly be used in the manufacture of compositions and, as will be evident from the above compilation, a wide range of known odorant substances or odorant substance mixtures can be used. In the manufacture of such compositions the known odorant substances enumerated above can be used according to methods known to the perfumer, such as e.g. from W. A. Poucher, *Perfumes, Cosmetics and Soaps* 2, 7th Edition, Chapman and Hall, London 1974.

#### EXAMPLE 1

(a) 92.8 g of potassium hydroxide and 1,46 l of ethanol (96%) are given into a 3 necked flask, equipped with a refrigerator, a dropping funnel and a thermometer. The outside is cooled with water and there is added within 1 hour at room temperature, 517 g of 30% aqueous formaldehyde. There are now added, within 1 hour, under stirring and at a temperature of 20°-25° C., 275 g (1,65

moles) of 2-formyl-caran. Agitation is continued for 3 hours at room temperature. Neutralisation of the medium is effected by the addition of 95 ml of acetic acid (pH 5-6), the refrigerator is replaced by a Vigreux column followed by a refrigerator, and the alcohol is distilled off at atmospheric pressure. There are obtained 1,55 l of distillate. The reaction product is cooled, taken up in 200 ml of methylene chloride added through the dropping funnel, decanted, the aqueous layer is extracted with 2×100 ml of methylene chloride; the combined organic layers are washed with 2×100 ml of sodium chloride solution, the organic layers are dried using sodium sulfate. The concentration is effected by means of a rotary evaporator, the final pressure is 20 mmHg. There are obtained 256,5 g of crude reaction product. A distillation step leads to 195 g of 2-[bis-(hydroxymethyl)]caran, b.p. 107°-108° C./0,1 mmHg, m.p. 70°-71° C.

(b) 154 g (0,77 moles) of 2-[bis-(hydroxymethyl)]caran, 773 g of acetone and 1,6 g of p-toluene sulfonic acid are given into a 2 l 3 necked flask, equipped with mechanical stirrer, a refrigerator and a thermometer. The mixture is stirred for 2 hours at room temperature. There are now added 16 g of solid sodium carbonate, this addition is followed by a 30 minutes agitation period. A filtration step is followed by distilling off the acetone on a rotary evaporator, the final pressure being 20 mmHg. The 179 g crude material are fractionated at 0,1 mmHg. There are obtained 161 g of 2,2,3',7',7'-pentamethyl-spiro[1,3-dioxane-5,2'-norcaran].

#### EXAMPLE 2

(a) 39 g of potassium hydroxide and 530 ml of 96% ethanol are given into a 3 necked flask, equipped with a mechanical stirrer, an ascending refrigerator, a 250 ml dropping funnel and a thermometer. An outside water circulation is effected and there are added, within 30 minutes, 188 g of 30% aqueous formaldehyde. Within 15 minutes, there are added at 20°-25° C. 100 g of 4-formyl-caran. Stirring is maintained for 3 hours at 20°-25° C. 2,8 ml of 90% aqueous acetic acid are added, the alcohol is distilled off, the reaction mass is cooled, the aqueous layer is decanted and washed with methylene chloride. The combined organic phases are washed with sodium chloride solution. The solvent is distilled, finally at a pressure of 20 mmHg. There are obtained 97,2 g of 4-[bis-(hydroxymethyl)]caran, having a melting point of 65°-66° C.

(b) 39,6 g of 4-[bis-(hydroxymethyl)]caran, 198 g of acetone and 1 g of p-toluene sulfonic acid are given into a 500 ml flask. There follows stirring for 2 hours at room temperature. Neutralisation of the reaction medium is effected by means of 3 g of sodium carbonate. There follows a filtration step, and distillation of the excess acetone. The crude reaction product is fractionated at a pressure of 0,5 mmHg. There are obtained 38,3 g of 2,2,3',7',7'-pentamethyl-spiro[1,3-dioxane-5,4'-norcaran]; b.p. 75°-76° C./0,5 mmHg.

Further compounds I' were obtained from the relevant compounds II as follows:

TABLE

R	R <sup>1</sup>	catalyst	physical data	odor
CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	pTSOH, H <sub>2</sub> O	b.p. = 75,77° C./0,05 mmHg n <sub>D</sub> <sup>20</sup> = 1.4809	amber, lactone, woody, slightly milky; powerful, tenacious.
C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	pTSOH, H <sub>2</sub> O	b.p. = 91° C./0,01 mmHg n <sub>D</sub> <sup>20</sup> = 1.4852	amber, woody, milky, slightly flowery; powerful, tenacious.

This Page Blank (uspic,

TABLE-continued

R	R <sup>1</sup>	catalyst	physical data	odor
H	H	H <sub>2</sub> SO <sub>4</sub> *	b.p. = 71.74° C./0.1 mmHg n <sub>D</sub> <sup>20</sup> = 1.4879	amber, woody, slightly lactone, animal side-note; powerful, tenacious.
H	C <sub>2</sub> H <sub>5</sub>	HCl conc.	b.p. = 83.87° C./0.2 mmHg n <sub>D</sub> <sup>20</sup> = 1.4795	amber, woody, agreeable roasted side-note; powerful, tenacious.
H	C <sub>3</sub> H <sub>7</sub>	HCl conc.	b.p. = 95-100° C./0.1 mmHg n <sub>D</sub> <sup>20</sup> = 1.4778	woody, green flowery, amber note developing on evaporation; powerful, tenacious.
H	CH <sub>3</sub>	HCl gaseous or H <sub>2</sub> SO <sub>4</sub> *	b.p. = 80° C./0.6 mmHg n <sub>D</sub> <sup>20</sup> = 1.4788	rich amber, woody and flowery side notes; powerful, tenacious.

\*using the acetal CH<sub>3</sub>CH(OEt)<sub>2</sub> of the carbonyl compound II

## EXAMPLE 3

	parts per weight
<b>A. Perfume concentrate (tobacco)</b>	
lemon oil furocoumarin-free	90
bergamot oil furocoumarin-free	200
lavandin oil	80
juniper berries-essence	20
geranium oil Bourbon	20
cinnamon oil	25
linalyl acetate	50
rosmarin oil	30
linalool	15
phenylethyl dimethyl-carbinyl acetate	50
Rose base substitute	10
isobornyl acetate	20
methyl n-nonylacetalddehyde	10
styrallyl acetate	10
citronellol	15
12-oxahexadecanolide	10
coumarin	30
Kephalis ® [4-(1-ethoxy-vinyl)-3,3,5,5-tetramethyl-cyclohexanone and its ethyl enol ether]	15
cedryl acetate	20
Lilial ® (p-tert. butyl-α-methyl-hydrocinnamic aldehyde	15
Irisantheme ® (mixture of methyl-ionones)	25
sandalwood oil East Indian	20
acetyl cedrene	30
oak moss absolute	20
Musk ketone (2,6-dinitro-3,5-dimethyl-4-acetyl-tertiary-butylbenzene)	40
patchouli oil	10
compound I', R=R <sup>1</sup> =CH <sub>3</sub>	30
diethyl phthalate	50
1,1-dimethyl isohexanol	40
	1000
<b>B. Concentrate for soaps (Fougere)</b>	
styrallyl acetate	10
bergamot oil substitute	200
benzyl acetate	50
Argeolene ®	30
patchouli oil substitute	30
cedarwood oil American	30
vetiver oil substitute	20
oak moss resinoid	40
musk ketone	40
benzyl salicylate	50
coumarin	80
geranium oil substitute	100
Sandela ® (3-isocamphyl-(5)-cyclohexanol)	100
compound I', R=H; R <sup>1</sup> =C <sub>2</sub> H <sub>5</sub>	20
Kephalis ®	50
diethyl phthalate	150
	1000
<b>C. Concentrate for foam bath (lemon)</b>	

-continued

	parts per weight
bergamot oil substitute	150
lemon oil substitute	340
C <sub>12</sub> -aldehyde (MNA)	30
petitgrain oil substitute	40
musk ketone	70
orange oil Brazil dest.	200
mandarin oil substitute	100
geranonitrile	30
2,2,6-trimethyl-6-vinyltetrahydrofuran	30
compound I', R=H; R <sup>1</sup> =CH <sub>3</sub>	10
	1000

I claim:

1. A compound of the general formula



wherein R and R<sup>1</sup> are H, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>, C<sub>3</sub>H<sub>7</sub> or CH(CH<sub>3</sub>)<sub>2</sub> and the sum of the carbon atoms in R and R<sup>1</sup> does not exceed 6, and X is caran-yliden (2,2) or caran-yliden (4,4).

2. A compound according to claim 1, which is 2,2,3',7',7'-pentamethyl-spiro[1,3-dioxane-5,2'-norcaran].

3. A compound according to claim 1, which is 2,3',7',7'-tetramethyl-spiro[1,3-dioxane-5,2'-norcaran].

4. A compound according to claim 1, which is 3',7',7'-trimethyl-2-ethyl-spiro[1,3-dioxane-5,2'-norcaran].

5. A compound according to claim 1, which is 2,3',7',7'-tetramethyl-2-ethyl-spiro[1,3-dioxane-5,2'-norcaran].

6. A compound according to claim 1, which is 3',7',7'-trimethyl-2,2-diethyl-spiro[1,3-dioxane-5,2'-norcaran].

7. A compound according to claim 1, which is 3',7',7'-trimethyl-spiro[1,3-dioxane-5,2'-norcaran].

8. An odorant composition containing a compound of the general formula



65 wherein R and R<sup>1</sup> are H, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>, C<sub>3</sub>H<sub>7</sub> or CH(CH<sub>3</sub>)<sub>2</sub> and the sum of the carbon atoms in R and R<sup>1</sup> does not exceed 6, and X is caran-yliden (2,2) or caran-yliden (4,4).

\* \* \* \* \*

This Page Blank (uspio)

# United States Patent [19]

Matsushita et al.

[11] Patent Number: 4,841,075

[45] Date of Patent: Jun. 20, 1989

[54] METHOD OF PREPARING ACETAL OR KETAL

[75] Inventors: Hajime Matsushita, Yokohama;  
Makoto Shibagaki, Kawasaki; Kyoko  
Takahashi, Tokyo; Hideyuki Kuno,  
Yokohama, all of Japan

[73] Assignee: Japan Tobacco, Inc., Tokyo, Japan

[21] Appl. No.: 129,702

[22] Filed: Dec. 7, 1987

[30] Foreign Application Priority Data

Dec. 11, 1986 [JP] Japan ..... 61-293470

[51] Int. Cl.<sup>4</sup> ..... C07D 317/00; C07D 317/22

[52] U.S. Cl. .... 549/341; 549/336;  
549/337; 549/429; 568/591; 568/594

[58] Field of Search ..... 549/429, 337, 336, 341;  
568/591, 594

[56] References Cited

U.S. PATENT DOCUMENTS

3,056,817	10/1962	Werber et al. ....	549/341
3,725,438	4/1973	Barone et al. ....	549/341
3,769,303	10/1973	Easter et al. ....	549/341
4,173,570	11/1979	Cleare ..... ..	549/341
4,289,700	9/1979	Yoshida et al. ....	549/341
4,518,785	5/1985	Eckhardt et al. ....	568/594
4,579,980	4/1986	Kogoma et al. ....	568/594

Primary Examiner—Asok Pal

Attorney, Agent, or Firm—Nixon & Vanderhye

[57] ABSTRACT

A method of preparing an acetal or ketal from a corresponding aldehyde or ketone is disclosed. A hydrous oxide of an element of Group IV of the Periodic Table is used as a catalyst, and the aldehyde or ketone is caused to react with an alcohol. The hydrous oxide can be obtained by partially dehydrating a hydroxide of the corresponding element. The method does not require an acid catalyst and is applicable to a carbonyl compound which is not stable in acids.

5 Claims, No Drawings

This Page Blank (uspio)

## METHOD OF PREPARING ACETAL OR KETAL

### BACKGROUND OF THE INVENTION

#### 1. Field of the Invention

The present invention relates to a method of preparing an acetal or a ketal and, more particularly, to a method of preparing an acetal or ketal by causing an aldehyde or ketone to react with an alcohol in the presence of a catalyst.

#### 2. Description of the Prior Art

When used in a variety of reactions, an acetal group or a ketal group is less reactive than a carbonyl group and can be easily converted into a carbonyl group. For this reason, when an aldehyde or a ketone is to be used in a desired reaction, it is first converted into an acetal or ketal. After the reaction has taken place, the reaction product is then converted into an aldehyde or ketone. That is to say, the acetal or ketal is very important as a protection group of the carbonyl group. An acetal or ketal is also important as a source material for synthetic perfume.

An acetal or ketal can be obtained by any one of the following reactions: acetylene reacting with an alcohol, an organometallic compound with an orthoester, vinyl ether with an alcohol, or a gem-dihalide with a metal alcoholate.

A more popular method of preparing an acetal or ketal is one in which an aldehyde or a ketone is used as a starting material and converted into a corresponding acetal or ketal. This method employs a synthesis reaction, for example, in which an aldehyde or ketone is made to react with an orthoester. However, the orthoester is expensive and is not easily available.

Therefore, another synthesis reaction is more often employed, in which an aldehyde or ketone is allowed to react with an alcohol. This synthesis reaction is performed in a solvent such as benzene in the presence of an acid catalyst. Water, which occurs as a by product, is removed by azeotropic distillation. Typical acid catalyst is a mineral acid (e.g., sulfuric acid or a p-toluene-sulfonic acid) or its derivative, although in recent years, an organic acid which is soluble in organic solvents has also come into use for the same purpose. Use of this method, however, presents the following problems:

First, since the synthetic reaction takes place in a homogeneous solution, a number of complicated operations must be performed, following the reaction, in order to isolate the product thereof. In particular, since the acid used as a catalyst is strong, a large quantity of alkaline water must be used to neutralize the solution, in order to separate the catalyst. Thus, a cooling operation is required, in order to eliminate the heat produced in the neutralizing process, and also a liquid separation operation.

Second, since a strong acid catalyst is used, the reaction vessel tends to become corroded, and the heating required in this reaction merely accelerates the corrosion process.

Third, since a strong acid is used as the catalyst, an aldehyde or ketone (e.g., 4-hydroxy-2-butanone) which is not stable in acidic conditions cannot be used as a starting material.

### SUMMARY OF THE INVENTION

It is an object of the present invention to provide a low-cost method of preparing an acetal or a ketal, wherein an aldehyde or ketone can be made to react

sufficiently with an alcohol in neutral conditions, and the product thereof can be isolated without the need for complicated treatment operations after the reaction is completed.

According to the present invention, there is provided a method of preparing an acetal or ketal, which comprises causing an aldehyde or ketone to react with an alcohol by using as a catalyst a hydrous oxide of an element of Group IV of the Periodic Table, thereby obtaining an acetal or ketal corresponding to the aldehyde or ketone.

The hydrous oxide used as the catalyst in the present invention is a rigid, solid material which is physically and chemically stable, and is obtained by partially dehydrating the hydroxide of the corresponding element. It is insoluble in water, alcohols, or any other organic solvents, as well as being chemically and thermally stable and inexpensive to produce. It is also highly active as a catalyst for accelerating a reaction between an aldehyde or ketone and an alcohol.

### DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

The most important characteristic feature of the present invention is the use, as a catalyst, of a hydrous oxide of an element of Group IV of the Periodic Table, zirconium hydrous oxide, titanium hydrous oxide, or tin hydrous oxide being the most preferable. The hydrous oxide of the selected element can be obtained as follows:

A hydroxide of the element is heat-treated under the conditions which do not allow dehydration of the hydroxide into a perfect oxide, so that the hydroxide is partially dehydrated. For example, when zirconium hydroxide is heated at a temperature of 500° C. or more at atmospheric pressure, it is completely dehydrated to obtain zirconia ( $ZrO_2$ ). However, when zirconium hydroxide is heated at about 300° C., zirconium hydroxide is partially hydrated to obtain a stable state. During the heat treatment, the weight of zirconium hydroxide is reduced by about 17% in about an hour, but subsequent weight loss rarely occurs. The same operations as described above can be performed for hydroxides of other elements other than zirconium.

The hydrous oxide is a rigid, white, solid material. Since it is also amorphous, it cannot be analyzed by X-ray diffraction, and thus its detailed chemical structure is not known. However, the chemical structure of the hydrous oxide can be assumed on the basis of the fact that the hydroxide is partially dehydrated. The hydrous oxide has an Elm-O-Elm bond (Elm represents an element of Group IV of the Periodic Table) formed by dehydration-condensation, and hydroxyl groups directly bonded to Elm atom are also present. As described above, the hydrous oxide is insoluble in water and organic solvents and is stable as a heterogeneous catalyst. The hydrous oxide does not cause problems such as elution and swelling and is excellent in heat resistance and solvent resistance. The hydrous oxide can be repeatedly used due to the above properties. In addition, the hydrous oxide is confirmed to have low surface acidity and good ion exchangeability with various ions.

The hydrous oxide can be easily obtained at low cost as follows. A hydroxide is obtained from minerals buried in a relatively large amount and is heat-treated and partially dehydrated to obtain the hydrous oxide. When this hydrous oxide is used as a catalyst, it may be pulver-

**This Page Blank (uspto)**

ized into grains having a proper size or may be supported on a proper carrier such as alumina, active charcoal, silica gel, silica-alumina, or zeolite.

The present invention can be properly embodied as follows.

The above catalyst, an aldehyde or ketone and an alcohol are mixed in a suitable vessel. The content of the aldehyde or ketone is 0.1 to 100 mmol and more preferably 1 to 10 mmol with respect to 1 g of the catalyst. The alcohol content is 0.4 to 1,000 mmol and more preferably 1 to 40 mmol with respect to 1 g of the catalyst. The volume of the solution is 5 to 100 ml and preferably 7 to 20 ml with respect to 1 g of the catalyst. If required, the solution can be diluted by an organic solvent (e.g., benzene or toluene) which does not react with the catalyst. The reaction solution is heated at a temperature falling within the range of room temperature to the boiling temperature of the solvent and is allowed to chemically react for a predetermined period of time. The optimal reaction time varies with the reaction temperature. After the reaction, the catalyst is removed by filtration. When the filtered solution is distilled, an acetal or ketal corresponding to the aldehyde or ketone as the starting material can be obtained.

Preparation of the catalyst used in the present invention, and preparation of an acetal or ketal according to the present invention will now be described in detail, by way of examples.

#### EXAMPLE 1

##### (Preparation of Catalyst)

In this example, 200 g of zirconium oxychloride (octahydrate) were dissolved in 10 l of deionized water, and a 1N sodium hydroxide aqueous solution was gradually added under stirring thereto to attain a pH of 6.80, as a result of which a hydrated gel of zirconium hydroxide was obtained. The resultant hydrated gel was filtered, and was washed with fresh deionized water. Washing continued until no chloride ions were detected in the filtrate. The resultant hydrated gel was dried and cut into pieces, and the pieces placed on a glass plate, and then dried. When the dried pieces were placed in deionized water, they rapidly broke up into grains of various sizes. The grains were filtered and separated from the water, and were dried in an enameled butt at room temperature, whereby 90 g of pulverized zirconium hydroxide were obtained.

Zirconium hydroxide grains having 24 to 60 mesh sizes were recovered and heated at 300° C. and atmospheric pressure for 3 hours, and were partially dehydrated, whereby zirconium hydrous oxide was obtained. The weight loss due to heating was approximately 17%.

#### EXAMPLE 2

##### (Preparation of Catalyst)

In this example, 10 l of deionized water were poured in a vessel, and 190 g of titanium tetrachloride were dissolved in the water under stirring. 28% aqueous ammonia solution was gradually added to control the pH value to 7. A hydrated gel of titanium hydroxide was precipitated and, the resultant hydrated gel was filtered through a Buchner funnel and then washed with deionized water until no chloride ions were detected in the filtrate. The resultant hydrated gel was cut into pieces by a knife, so as for the gel to dry more quickly. The pieces were then placed on a glass plate and dried at room temperature. When the dried pieces were

placed in deionized water, they quickly broke up into grains of various sizes. The grains were filtered and dried in an enameled butt at room temperature, whereby 30 g of pulverized titanium hydroxide were obtained.

Titanium hydroxide grains having 24 to 60 mesh sizes were recovered and heated at 300° C. and atmospheric pressure for 3 hours and were partially dehydrated, whereby titanium hydrous oxide was obtained.

#### EXAMPLE 3

##### (Preparation of Catalyst)

261 g of tin tetrachloride were added dripwise to 4 l of deionized water and 28% aqueous ammonia solution was gradually added thereto under stirring, to control a pH to 7, thereby precipitating a hydrated gel of tin hydroxide. The resultant hydrated gel was filtered through a Buchner funnel and was washed with deionized water until no chloride ions were detected in the filtrate. The resultant hydrated gel was cut into pieces by a knife, so as for the gel to dry more quickly. The pieces were placed on a glass plate and were dried at room temperature. When the dried pieces were placed in deionized water, they quickly broke up into grains of various sizes. The grains were filtered and dried in an enameled butt at room temperature, as a result of which 141 g of transparent, pulverized tin hydroxide were obtained.

Tin hydroxide grains having 24 to 60 mesh sizes were recovered and heated at 300° C. and atmospheric pressure for 5 hours and were partially dehydrated, whereby tin hydrous oxide was obtained.

#### EXAMPLE 4

##### (Preparation of Acetal by Ethylene Glycol)

0.5 g (0.5 mmol) of n-hexanal and 0.62 g (10 mmol) of ethylene glycol were dissolved in 10 ml of benzene in a 25-ml eggplant type flask. 1.0 g of the zirconium hydrous oxide prepared in Example 1 was added to the mixture. The resultant solution was heated by a mantle heater and slowly refluxed. After the solution had reacted for 4 hours, it was cooled and filtered to eliminate the catalyst. The solvent was then evaporated and subjected to reduced pressure distillation, whereby 0.71 g of n-hexanal ethyleneglycoxy acetal were obtained (yield: 98%).

#### EXAMPLE 5

##### (Preparation of Acetal and Ketal by Ethylene Glycol)

Acetals or ketals corresponding to various carbonyl compounds were prepared following the same procedures as in Example 4, except that the various carbonyl compounds and the ethylene glycol shown in Table 1 were used as starting materials.

In all the reactions, 1.0 g of the zirconium hydrous oxide as a catalyst, 5 mmol of each carbonyl compound, and 10 ml of the solvent were used. The reaction conditions were selected from among A, B, and C.

A: reflux in a benzene for 4 hours

B: reaction in tetrahydrofuran at room temperature for 20 hours

C: reaction in benzene with azeotropic dehydration for one hour

The products were analyzed by gas chromatography. The results of the analysis are summarized in Table 1.

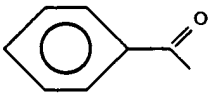
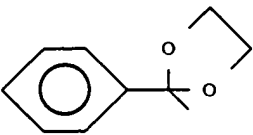


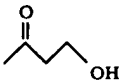
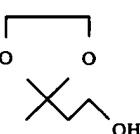
This Page Blank (uspto,

TABLE I

CARBONYL COMPOUND	PRODUCT ACETAL OR KETAL	CARBONYL:ETHYLENE GLYCOL	REACTION CONDITION	YIELD (%)
		1:1	A	90
"	"	1:2	B	65
		1:2	A	92
		1:2	A	98
		1:2	A	72
		1:2	C	80
		1:2	A	80
		1:1	A	74
"	"	1:2	A	90
"	"	1:2	B	72
"	"	1:1	C	83
		1:2	B	31
		1:2	B	79
		1:1	A	32
		1:1	A	80

**This Page Blank (uspto)**

TABLE 1-continued

CARBONYL COMPOUND	PRODUCT ACETAL OR KETAL	CARBONYL:ETHYLENE GLYCOL	REACTION CONDITION	YIELD (%)
		1:2	A	30
		1:2	A	15
		1:2	B	28

## EXAMPLE 6

(Preparation of Acetal by Methanol or Ethanol)

10 ml of methanol or ethanol were added to 0.5 g (0.5 mmol) of n-hexanal in a 25-ml eggplant type flask. 1.0 g of zirconium hydrous oxide prepared in Example 1 was added to the mixture. The resultant solution was heated by a mantle heater and slowly refluxed for 4 hours.

The reaction products were analyzed by gas chromatography, and the following result was obtained:

The reaction product obtained by using methanol was n-hexanal dimethylacetal (yield: 100%), and that obtained by using ethanol was n-hexanal diethylacetal (yield: 91%).



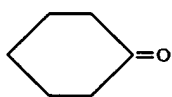
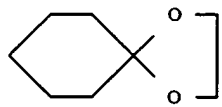


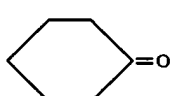
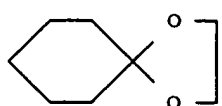

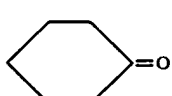
## EXAMPLE 7

(Preparation of Acetal or Ketal by Various Catalysts)

Acetals were prepared in the same procedure as in Example 1, by using n-hexanal and ethylene glycol and various catalysts. Ketals were prepared using cyclohexanone and ethylene glycol. The results of product analysis are summarized in Table 2.


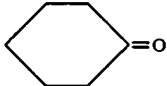
The titanium hydrous oxide and tin hydrous oxide used as the catalysts were as prepared in Examples 2 and 3, respectively. Commercially available active alumina and silica for chromatography were used as comparative catalysts.

TABLE 2

CARBONYL COMPOUND	PRODUCT ACETAL OR KETAL	CATALYST	YIELD (%)
		TITANIUM HYDROUS OXIDE	83
		"	87
		TIN HYDROUS OXIDE	34
		"	39
	—	ACTIVE ALUMINA	0
	—	"	0

This Page Blank (uspto)

TABLE 2-continued

CARBONYL COMPOUND	PRODUCT ACETAL OR KETAL	CATALYST	YIELD (%)
 CHO	—	SILICA FOR CHROMATOGRAPHY	0
 =O	—	SILICA FOR CHROMATOGRAPHY	0

According to the method of the present invention as described above, the acid catalyst need not be used, and the acetal or ketal can be prepared from a carbonyl compound (e.g., 4-hydroxybutanone) which is unstable in acids. Various other advantages can be provided by the invention. For example, the catalyst can be used repeatedly.

What is claimed is:

1. A method of preparing an acetal or ketal, which comprises causing an aldehyde or ketone to react with an alcohol by using a hydrous oxide of an element of Group IV of the Periodic Table as a catalyst, whereby the acetal or ketal corresponding to the aldehyde or ketone is obtained.

2. A method according to claim 1, wherein the catalyst is one selected from the group consisting of a zirconium hydrous oxide, a titanium hydrous oxide, and a tin hydrous oxide.

3. A method according to claim 1, wherein the hydrous oxide pulverized into grains having a desired size is used without further modifications.

4. A method according to claim 1, wherein the hydrous oxide is carried on a suitable carrier selected from the group consisting of alumina, active charcoal, silica gel, silica-alumina, and zeolite.

5. A method according to claim 1, wherein the catalyst is used repeatedly.

\* \* \* \* \*

30

35

40

45

50

55

60

65

This Page Blank (uspto)

[54] PROCESS FOR THE PREPARATION OF  
SESQUITERPENE KETONES

3,647,847 3/1972 Curtis et al. .... 260/587  
3,718,698 2/1973 Hall ..... 260/587

[75] Inventors: Harmannus Boelens, Huizen; Petrus  
C. Traas, Naarden, both of  
Netherlands

*Primary Examiner*—Bernard Helfin  
*Assistant Examiner*—Norman Morgenstern  
*Attorney, Agent, or Firm*—Stevens, Davis, Miller &  
Mosher

[73] Assignee: Naarden International NV,  
Naarden-Bussum, Netherlands

[22] Filed: July 17, 1973

[21] Appl. No.: 380,054

[30] Foreign Application Priority Data

July 20, 1972 United Kingdom..... 33960/72

[52] U.S. Cl. .... 260/586 P; 260/586 G; 260/586 F

[51] Int. Cl. .... C07c 45/04

[58] Field of Search..... 260/587, 586 B, 586 P

## [57] ABSTRACT

A process for the preparation of sesquiterpene ketones, which includes reacting, at 40° to 100°C. for from 6–12 hours, a sesquiterpene hydrocarbon having one olefinic linkage in the endocyclic position with hydrogen peroxide in the presence of a lower alkyl formate such as ethyl formate.

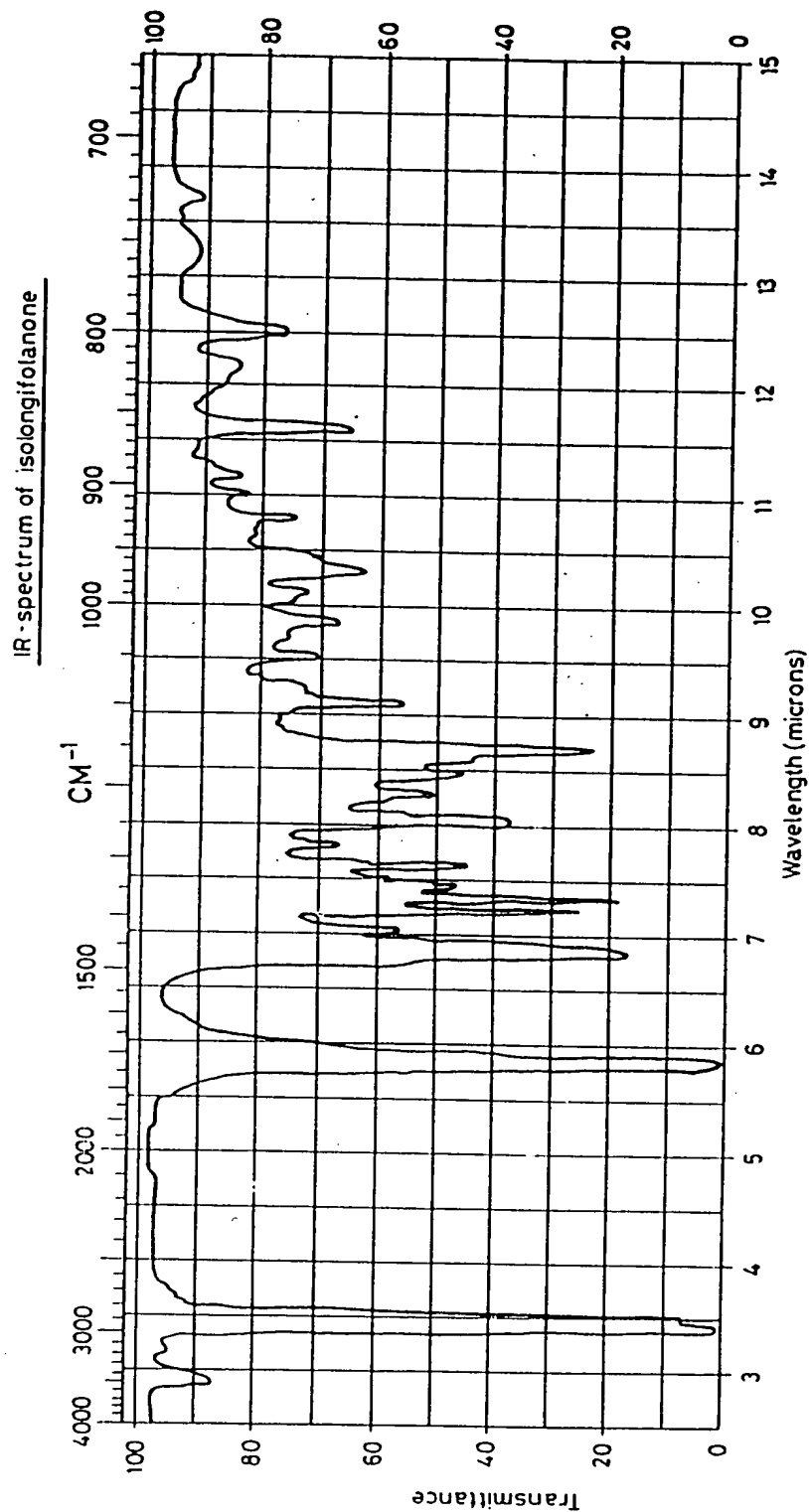
[56] References Cited

UNITED STATES PATENTS

2,555,927 6/1951 Himel et al. .... 260/618 R

3 Claims, 4 Drawing Figures

This Page Blank (uspto)

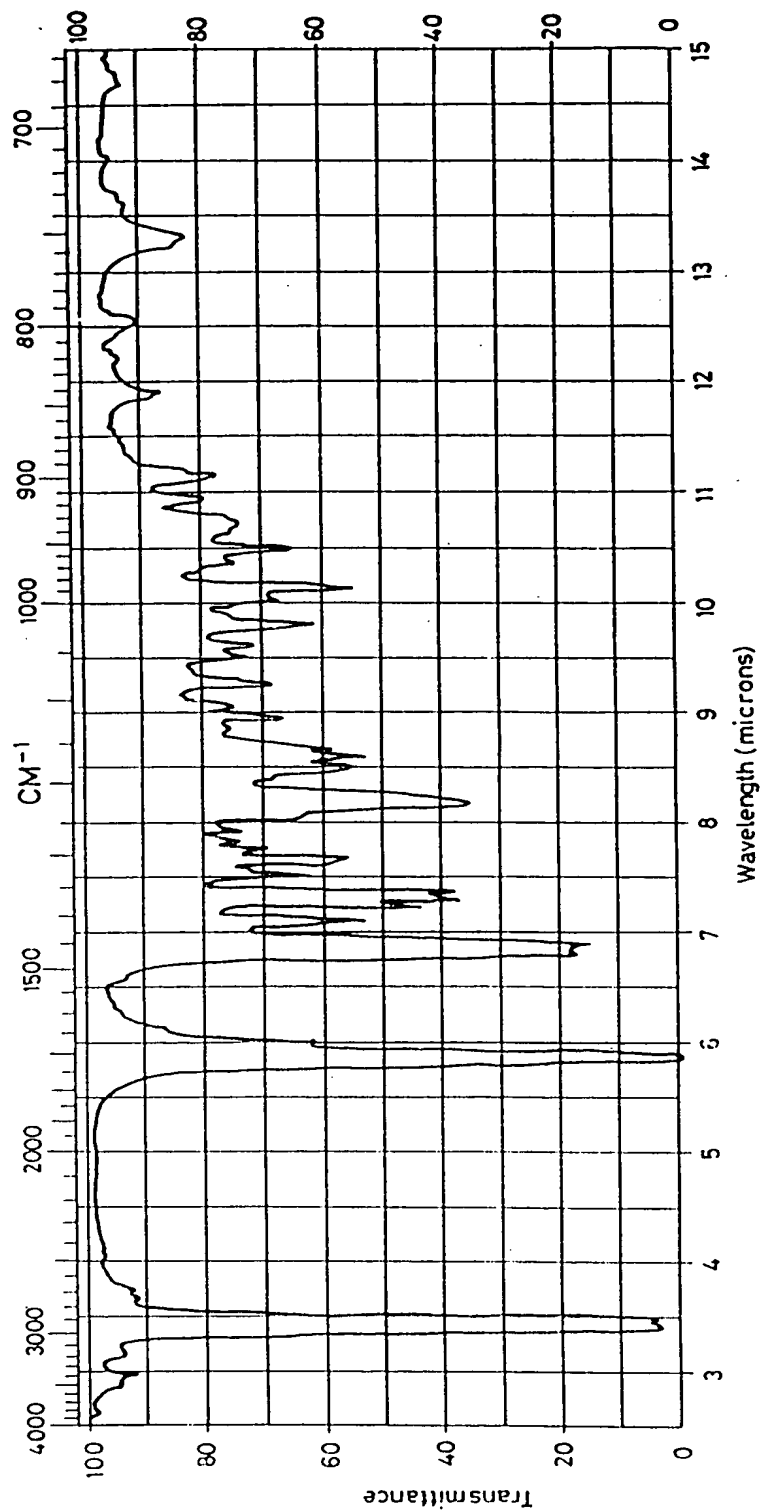
FIG - 1

Phase: 100 %, Thickness: 0.020 mm  
Instrument: Perkin Elmer 137 E (infracord)

This Page Blank (uspto)

Fig. 2

IR - spectrum of cedranone

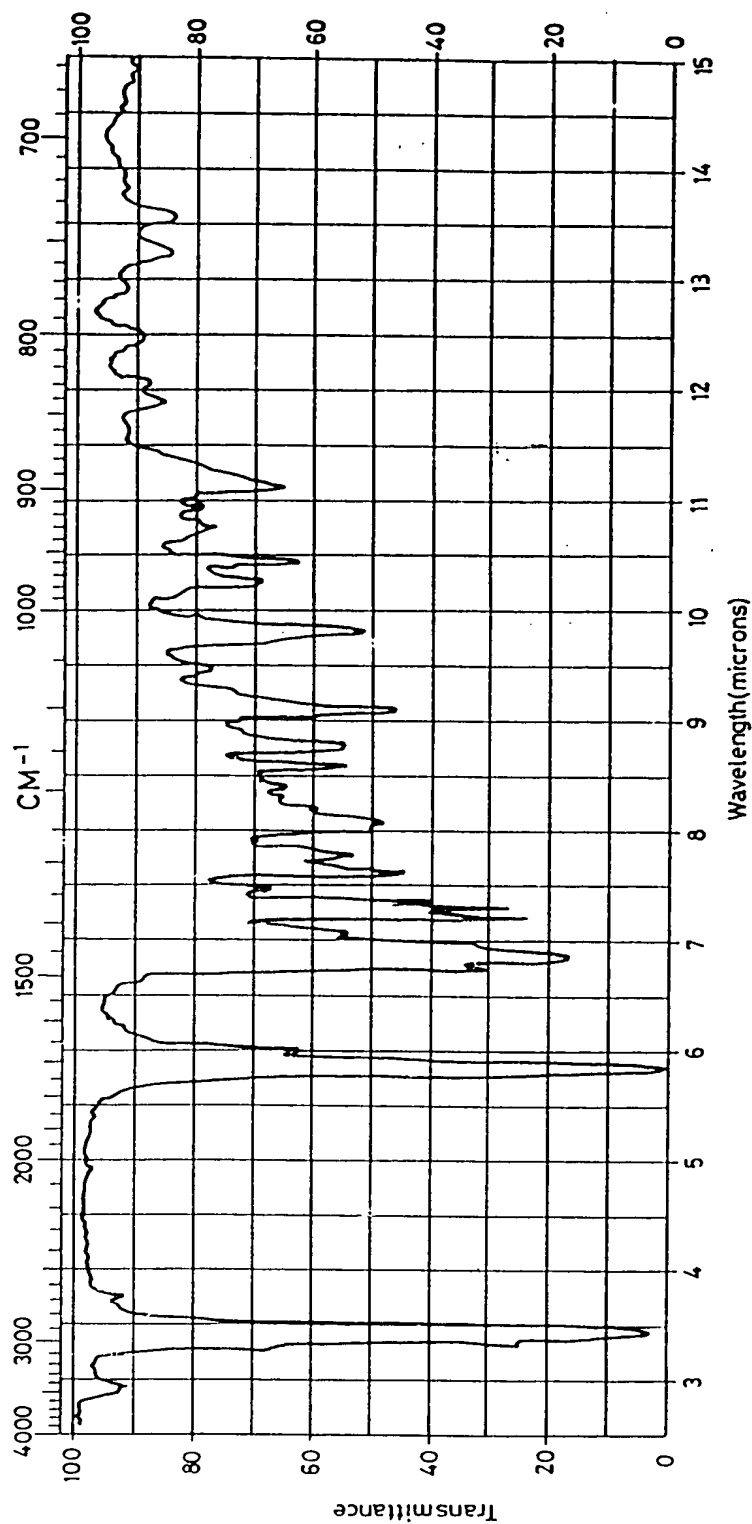


Phase: 100 %, Thickness: 0,020 mm  
Instrument: Perkin Elmer 137 E (infracord)

This Page Blank (uspto)

**FIG. 3**

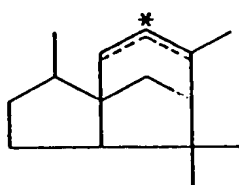
IR-spectrum of thuyopsanone



Phase: 100% Thickness: 0.020 mm  
Instrument: Perkin Elmer 137 E (infracord)

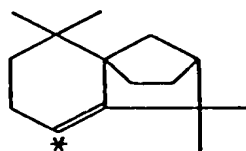
This Page Blank (uspto)

1.



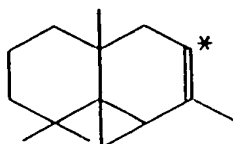
Cedrene

2.



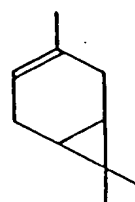
Isolongifolene

3.



Thuyopsene

4.



Delta-3-carene

This Page Blank (uspto)

# PROCESS FOR THE PREPARATION OF SESQUITERPENE KETONES

The invention relates to a process for the preparation of sesquiterpene ketones.

More particularly the invention provides a process for the oxydation of sesquiterpene hydrocarbons, containing a single ethylenic bond, with the aid of hydrogen peroxide in such a way that sesquiterpene ketones free from isomeric ketones are obtained.

Although oxygen-containing sesquiterpene derivatives have found an increasing interest in the fragrance and flavour industry the number of sesquiterpene ketones actually used is still very small. S. Aretander, *Perfume and Flavor Chemicals*, Montclair, N.J. (1969) describes only cedranone (monograph no. 596), germacrene (no. 1463), nootkatone (no. 2382) and vetivone (no. 3089).

The increased interest is also reflected in some recent patent applications. The British Pat. Specification No. 1,197,579 discloses the use of an oxydation product of isolongifolene as an ingredient in perfume compositions.

The product is obtained by the oxydation of isolongifolene with sodium bichromate in acid medium and consists of a mixture of at least three ketones. Oxydation with hydrogen peroxide and  $V_2O_5$  in acetone again leads to a mixture of ketones together with unreacted isolongifolene. No yields have been mentioned.

The British Pat. Specification No. 1,216,048 covers the preparation and use as a fragrance material of novel thuyopsanones obtained from thuyopsene.

According to this patent application the oxydation of thuyopsene is preferentially performed with peracetic acid or chromylchloride but other reagents such as  $MnO_2$ ,  $KMnO_4$  and oxygen in combination with actinic radiation may be used as well. The yield of thuyopsanone isomers obtained is 70% of the theoretical value in the case of peracids, whereas yields of 35.4% and 30% are obtained when chromylchloride or oxygen are used.

It has now been found that high yields of sesquiterpene ketones are obtained when suitable sesquiterpene hydrocarbons are reacted with hydrogen peroxide in the presence of a lower alkylformate. No allylic oxydation occurs.

It is known from U.S. Pat. No. 2,555,927 that unsaturated organic compounds on treatment with hydrogen peroxide and an alkyl formate boiling below 100°C as a catalyst yield vicinal diols. The reaction applies to the hydroxylation of olefinic linkages in monoolefins, diolefins, unsaturated fatty acids, unsaturated alcohols, olefins substituted with a cyclic structure and to cyclic olefins which may be substituted by a saturated group.

In contrast to this it was found the sesquiterpene hydrocarbons  $C_{15}H_{24}$ , containing one olefinic bond in endocyclic position, on treatment with hydrogen peroxide and a lower alkyl formate, under reaction conditions which deviate from those claimed in U.S. Pat. No. 2,555,927, do not yield vicinal diols but give rise to the formation of sesquiterpene ketones.

Examples of sesquiterpene hydrocarbons  $C_{15}H_{24}$ , which contain one olefinic linkage and follow the process of the invention are cedrene, isolongifolene, thuyopsene and the like (formula 1, 2, and 3 resp.).

Sesquiterpene hydrocarbons containing more than one olefinic linkage such as beta-caryophyllene, when reacted according to the invention, produce a mixture

of unidentified compounds besides much polymeric material.

It was also found that sesquiterpene hydrocarbons containing one olefinic linkage in exocyclic position do not produce a carbonyl compound.

Comparison of related structures in the process of the invention, e.g. thuyopsene with delta-3-carene (formula 4) shows that with monoterpenes side reactions, such as opening of the cyclopropane ring and polymerisation, occur whereas the sesquiterpenes give a high yield of ketones.

The invention is therefore limited to sesquiterpene hydrocarbons containing one olefinic linkage in endocyclic position.

The preferred reaction conditions leading to diols according to U.S. Pat. No. 2,555,927 comprise the use per mol olefin of 1.1-1.2 moles of hydrogen peroxide of 5-15% by weight concentration combined with 50-100 mol %, based on hydrogen peroxide, of low boiling alkyl formate, preferably methylformate, at a temperature in the range between 25° and 100°C in a period between 12 and 48 hours.

For the introduction of a keto group into sesquiterpene hydrocarbons according to this invention the following conditions apply:

1 mol of sesquiterpene hydrocarbon is reacted with 1.3-1.5 moles of hydrogen peroxide of a concentration of 20-50% by weight, a lower alkylformate chosen from the group of methyl-, ethyl-, propyl-, and butylformates, preferably ethylformate, in an amount of 120-200 mol % on hydrocarbon at a temperature in the range between 40° and 100°C, in period between 6 and 12 hours.

The process of the invention may be illustrated by the following examples.

## EXAMPLE I

A 6-liter glass reactor, equipped with a stirrer a dropping-funnel and a reflux condenser, is charged with 1,350 g. isolongifolene (6.6 moles) and 975 g. ethyl formate (13.2 moles). The contents are heated to about 57°C and 975 g. hydrogen peroxide (concentration 30% by wt., 8.6 moles) is added at such rate that no excessive foaming occurs. This takes between 1 and 2 hours after which refluxing is continued for another 6 hours. During the reaction the temperature in the bottom gradually increases to about 73°C. The reaction mass is then cooled to about 25°C, and the aqueous bottomlayer drained off and discarded. The toplayer is washed in succession with 900 ml. saturated sodium bicarbonate solution and 900 ml. water and then dried over anhydrous magnesiumsulphate. On fractionation under vacuum 1014 g. isolongifolanone bp 113°-117°C/2 mm.  $n_D^{20}$  = 1.5011 IR-spectrum FIG. 2 is obtained.

A panel of six trained perfumers was unanimously of the opinion that the odour of the isolongifolanone thus obtained is preferred to that of the isomeric mixture of ketones known as isolongifolene oxidate from British Patent Specification No. 1,197,579.

## EXAMPLE II

In a similar 1 liter reactor 204 g. (1 mol) cedrene, 165 g. 30% hydrogen peroxide (1.45 moles) and 150 g. ethyl formate are reacted as described in Example I. The temperature in the bottom increases from 58°C to 82°C in 6 hours. 154 g. cedranone bp 124°-126°C/O.2

This Page Blank (uspto)

mm;  $n_D^{20} = 1.5026$ ; IR-spectrum FIG. 2 is obtained.

### EXAMPLE III

Thuyopsene is reacted as in Example II. Temperature increases from 57° to 78°C in 10 hours. 195 g. thuyop- 5 sanone is obtained, bp 116°-122°C/1.8 mm;  $n_D^{20} = 1.5022$ ; IR-spectrum FIG. 3.

### EXAMPLE IV

The preparation according to example III is repeated, 10 but ethyl formate is replaced by butyl formate (1.5 moles) 182 g thuyopanone is obtained.

The formulae 1 to 4 referred to herein are shown in FIG. 4 of the accompanying drawings. FIGS. 1 to 3 of 15 the accompanying drawings show the infra-red spectra of the products of Examples I to III, respectively.

What we claim is:

1. A process for the preparation of sesquiterpene ketones comprising reacting at a temperature of 40° to 100°C. for a period of 6 to 12 hours 1 mol of sesquiterpene hydrocarbon having one olefinic linkage in an endocyclic position selected from the group consisting cedrene, isolongifolene and thuyopsene with 1.3 - 1.5 mols of hydrogen peroxide, having a concentration of from 20 - 50% by weight in the presence of from 120 - 200 mol % of a lower alkyl formate.

2. Process according to claim 1 wherein said lower alkyl formate is chosen from the group of methyl-, ethyl-, propyl-, and butylformates.

3. Process according to claim 2 wherein said lower 15 alkyl formate is ethyl formate.

20

25

30

35

40

45

50

55

60

65

*This Page Blank (uspto)*